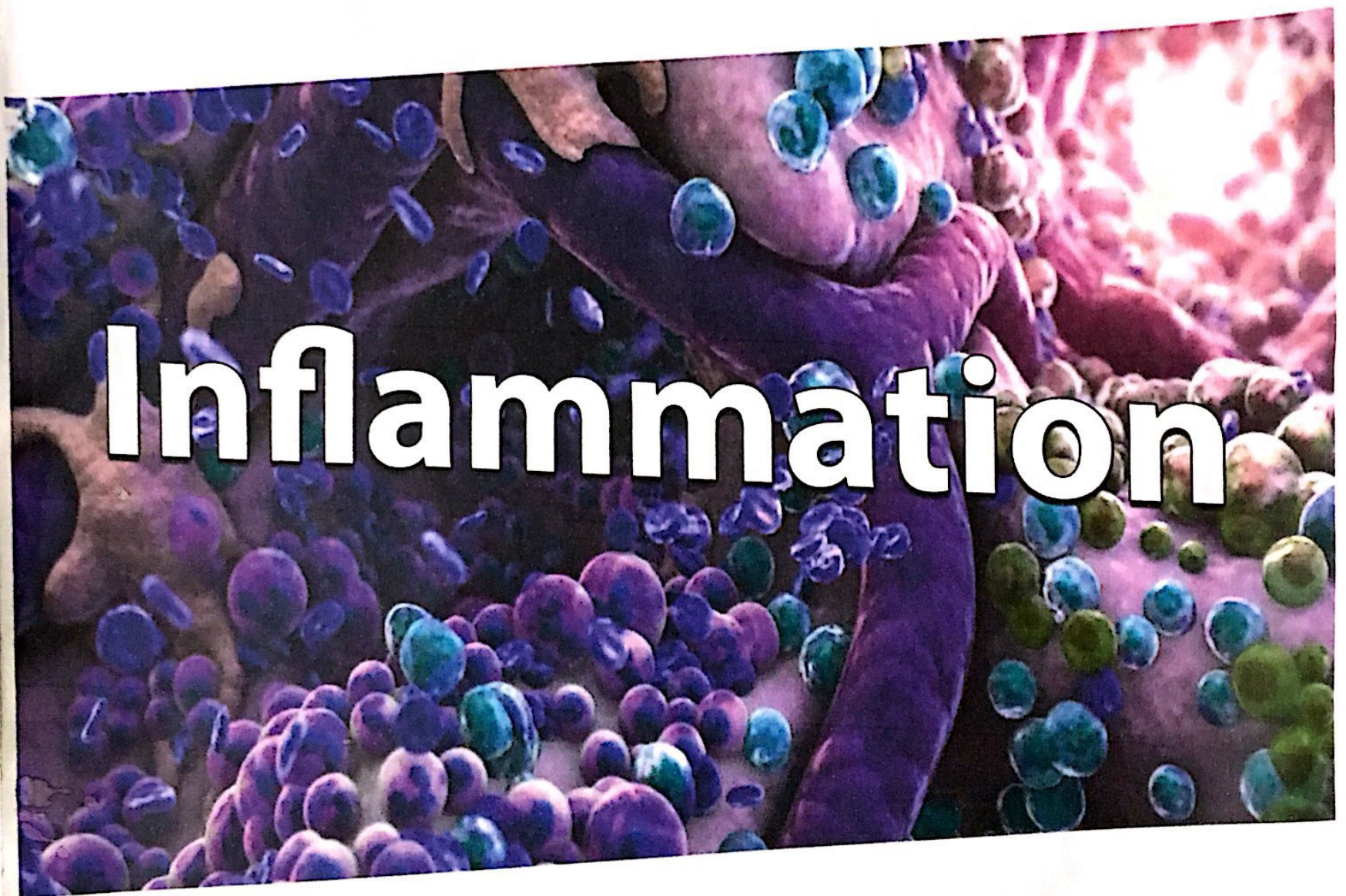


TIMS **Easy** **Pathology**

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Ainshams 2018 - 2019

VISIT...

LANZAROTE
Caliente.COM

Inflammation

protective response of living vascularized tissue against injury, to get rid of injury.

Aim: Removal of harmful agents - Removal of dead tissue - Prepare for healing

Pleurisy ← Pleura التهاب الجناب pneumonia ← lung التهاب الرئة

Acute	Chronic
Rapid onset	Gradual slow onset
Short duration (minutes to days)	Long duration (months - years)
More vascular reaction (redness and <u>fluid exudate</u>)	Less vascular reaction More <u>fibrosis</u>
More <u>neutrophils</u> <i>resistant phagocytes</i>	Lymphocytes, plasma cells & macrophages

Fulminant: Severe acute inflammation → *Flu like fever*
Chronic active: Chronic with acute exacerbations (attacks)
Subacute: between acute and chronic

Acute inflammation

Rapid response, which is sufficient to deliver high amount of neutrophils and plasma proteins to site of injury

Causes of acute inflammation:

- Infections:** viral - bacterial - fungal - parasitic
- Immunological:** Hypersensitivity - Autoimmune
- Physical:** Heat - Radiation (Ultra violet - ionizing radiation)
- Chemicals:** Acids - Alkalis - poisons
- Trauma**
- Tissue necrosis**
- Inert Foreign body** (splinter of wood, or sutures)

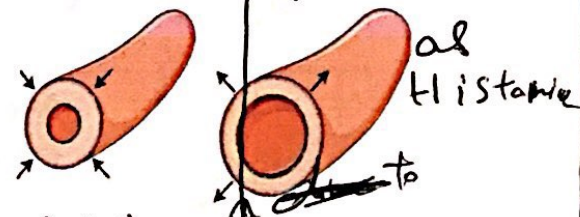
Reactions of acute inflammation (Pathogenesis)

Vascular changes - Cellular reaction

Vascular reaction: (of arterioles, capillaries, and venules)

1) Caliber changes:

- Transient **Vasoconstriction** of arterioles (few seconds to minutes)
- Progressive **Vasodilatation** (after 30 min.) more in arterioles
 - That leads to increased blood flow in the area of inflammation
 - Increased hydrostatic pressure → transudate fluid in tissue (fluid with low protein)



due to release of chemical mediators



and drainage slow

2) Increased permeability

○ Mechanisms:

- Endothelial cell **contraction** (by Histamine-Bradykinin-Leukotriens) → opening gaps of venules (**the commonest factor of permeability**)
- Endothelial cell **retraction in venules** (Cytokines IL-1, TNF) → changes in cytoskeleton of endothelial cells
- Endothelial cell **injury** (by leucocytes - irritants)

○ Permeability leads to:

- Fluid **exudate** (protein rich-fluid) formation
- Increased **osmotic pressure** in tissue → drag more fluid
- Increased blood viscosity → **stasis** (slow blood flow) → Neutrophil margination

3) Fluid Exudate formation

○ Pathogenesis:

- Increased **permeability** and vasodilatation
- Increased **hydrostatic** pressure inside b.v.
- Increased **osmotic** pressure outside b.v. (due to damage of proteins)

○ composition:

- Plasma + inflammatory cells + high content of **proteins** (>4 gm/dl)
- Proteins are mainly **Ig, Fibrinogen, Complement**

○ Function:

- Dilute toxins
- Antibodies (Ig) → opsonin, bacteriolysin, agglutinin → fix and destroy target
- **Fibrinogen** → **fibrin**
 - Fibrin forms a network for cell movement
 - Fibrin surrounds infection (**Localization**)
- Inflammatory cells → killing organisms & cleaning

○ Fate:

- Drained through lymphatic circulation → then to venous blood
- If infected → lymphangitis → lymphadenitis → may lead to bacteremia, toxemia, or even septicemia

Exudate	Transudate
More permeability	Less permeability
Turbid & clots on standing (fibrinogen)	Clear
Sp. Gravity 1018 or more	Sp. Gravity <1015
High protein >4gm/dl	Low protein < 4gm/dl
Inflammatory cells	no inflammatory cells



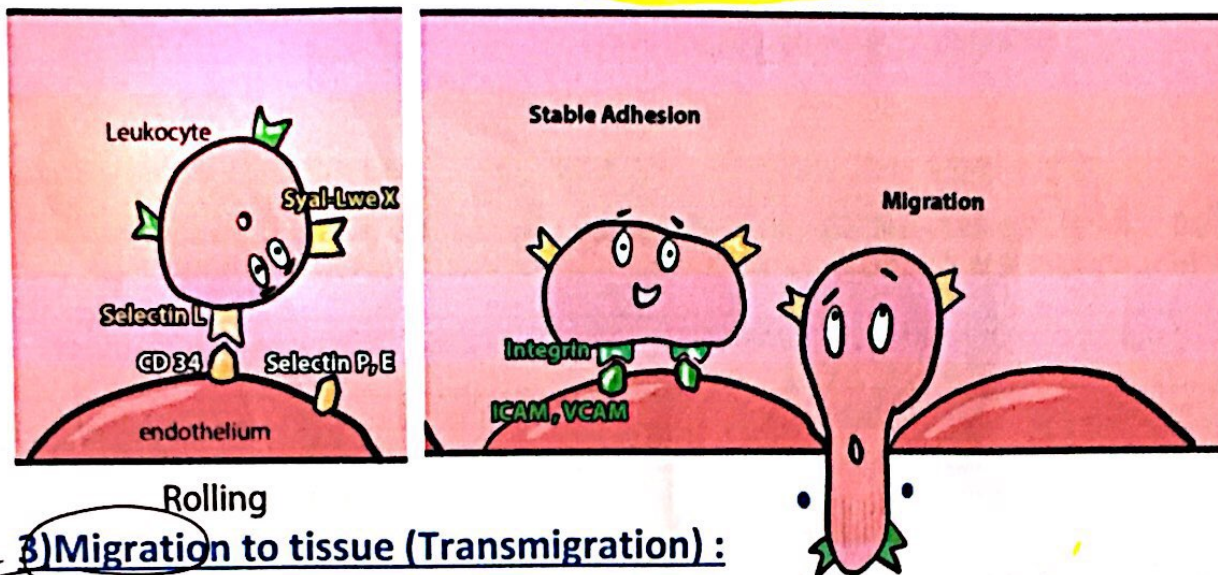
Cellular reaction & Recruitment

1) Margination & Rolling

- Leucocytes become peripheral due to **stasis**,
- Leucocytes bind **loosely** to endothelium and **roll** by **Selectin** family CD62 :
 - Leucocyte selectin receptor (L-selectin)
 - Endothelial selectin (P & E selectin)
 - Platelet selectin (P selectin)

2) Adhesion :

- Firm adhesion between (leucocyte **Integrin**) & (Endothelial **ICAM-1, VCAM-1**)
- These molecules are activated by **Cytokines (IL-1, TNF)** → expression of Integrins



3) Migration to tissue (Transmigration) :

- Leucocytes are leaving the blood vessel (mainly venules) through the gap
- Helped by:
 - PECAM-1** on leucocyte & endothelium
 - Pseudopodia formation (**diapedesis**)
 - Enzymatic degradation of **Basement membrane** by **collagenase**

4) Chemotaxis :

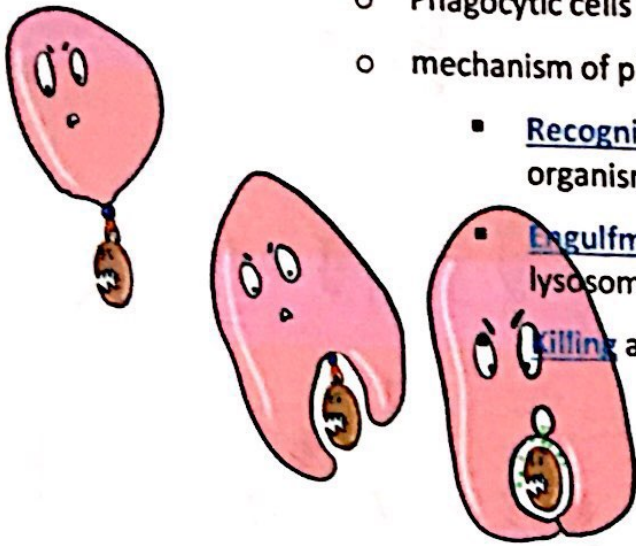
- Directed movement of leucocytes towards organism, or necrotic tissue
- Guided by:
 - Plasma Complement **C3a, C5a**
 - Cytokines (**IL-8**)
 - Leukotriene B4** (products of Arachidonic acid metabolism)
 - bacterial products** : e.g. **Cocci** attract neutrophils, **C3A, C5A, lymphokine**
 - e.g. **macrophage attracted by bacilli**, **C3a, C5a, lymphokine**

5) Activation of leucocytes stimulated by mediators (CK), necrosis, and microbes:

- Free radicals (FR) formation : ROS Reactive oxygen substances (e.g. H_2O_2) toxic to bacteria
- Lysosomal Enzymes formation
- Mediators secretion (e.g. arachidonic acid, CK)

6) Phagocytosis: ((Recognition and binding))

- Phagocytic cells are **Neutrophils**, **macrophage**, and **tissue histocytes**
- mechanism of phagocytosis :
 - Recognition and binding:** by **opsonins** (IgG + C3b) → coating organism → binding to leukocytes
 - Engulfment:** by pseudopods → forming vacuole → binds with lysosome → phagosome
 - Killing and degradation:** by :
 - Free radicals (ROS) e.g. H₂O₂
 - Reactive nitrogen, NO
 - Lysosomal enzymes e.g. defensin



Macrophage	neutrophils
Monocyte, or tissue histocytes <i>blood</i> ←	Polymorphnuclear leucocyte (PMNL)
Respond to inflammation within 1-2 days	Respond to inflammation within 6-24 h.
Found in acute and chronic inflammation	Found in acute inflammation
Long living cells may transform into: - Epithelioid cell - Giant cell - Foam cell	Fate: - Apoptosis - Pus cell (in case of pus formation)

درتجی سببه
epithelioid
cell

Chemical Mediators

Products of cells during inflammation or derived from plasma and activated. They act by receptor binding, then degraded by enzymatic cleavage.

By Function:

Histamine

Prostaglandin

N.O.

- Vasodilatation, Permeability
- Vasodilatation, Pain, Fever
- Vasodilatation, tissue damage

Substance P, serotonin

Bradykinin

Leukotrienes

- Permeability
- Permeability, Pain
- Permeability (C,D,E), Leukocyte activation (B)

pain → prostaglandin, bradykinin

Leukocyte recruitment and activation by C3a/C5a/IL-1//LB4/Bacterial products
tissue damage NO/ROS/Lysosomal enzymes

By Origin:

Compelement, Coagulation system & kinin

Serotonin

Others (Histamine, PAF, Pg, Lekotrin....) → from Mast cells & other cells (cell mediator)

N.B. (hitamine is normally present, while Pg is secreted in demand)

→ from **Liver** (plasma mediators)

→ from platelets (cell mediator)

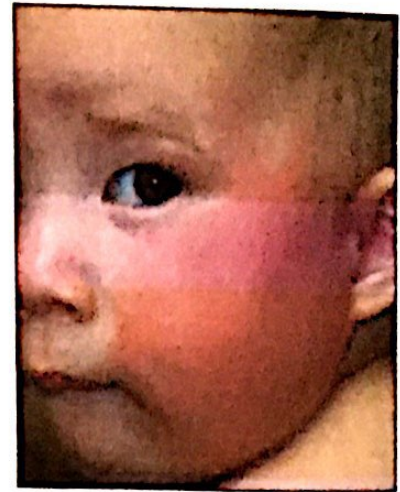
Fever → Vasodilatation

tissue necrosis

↓
ach 31

Local signs of Acute inflammation

- **Redness & hotness:** caused by vasodilatation & blood flow
- **Swelling :** caused by inflammatory exudate
- **Pain:** caused by Pg, Bradykinin, and exudate leads to stretching of tissue and irritation of nerves.
- **Loss of function :** caused by pain and swelling

Systemic effects of acute inflammation

'Acute phase reaction'

Most imp mediators are cytokine (TNF-IL-1&IL-6)

Fever (1-4 degrees more than normal):

- Bacterial exogenous pyrogens → stimulate leucocytes → secretion of endogenous pyrogens (Cytokines IL-1, TNF)
- Cytokines (IL-1, TNF) → increase Pg
- Pg → ++ transmitters in hypothalamus → resetting temperature

Leucocytosis ↑WBCs (15000-20000 cell/ul) due to B.M. stimulation by:

- Cytokines (IL-1, TNF) → release of cells from B.M. reserve
- Macrophage & lymphocytes → colony stimulation factor CSFs

Production of WBCs is highly selective in some cases:

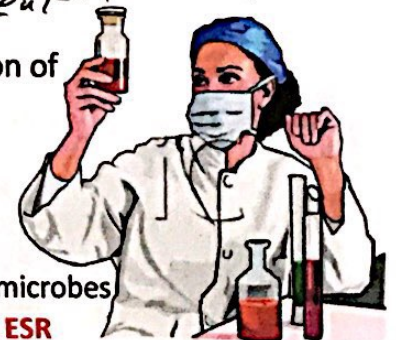
- Neutrophilia in case of bacterial infection
- Eosinophilia in parasitic infection or allergy
- Lymphocytosis in viral infection
- monocytosis → typhoid

N.B. Certain infections (e.g. typhoid) → Leukopenia due to migration of lymphocytes to L.N.s

○ Liver activation → Acute phase proteins (>100 folds)

Cytokines (IL-6) → hepatocytes activation → secrete:

- CRP & serum amyloid A (SSA) → opsonization of microbes
- Fibrinogen → bind to RBCs (rouleaux) → elevated ESR

○ Lymphangitis & lymphadenitis reaction to drained exudate○ Shock & DIC → Disseminated intravascular coagulation

- High amounts of CK (TNF) → systemic V.D. → hypotension
- High amounts of CK (TNF) → activated coagulation → microthrombi → disseminated intravascular coagulation DIC

○ Others **DRAFT**

- **Dry skin** (less cutaneous blood, less sweating)
- **Rigors (shivering)** : feeling cold due to heat resetting
- **Anorexia**: due to effect of (TNF) on appetite center
- **Fatigue & malaise** (cytokines)
- **Tachycardia and hypotension**

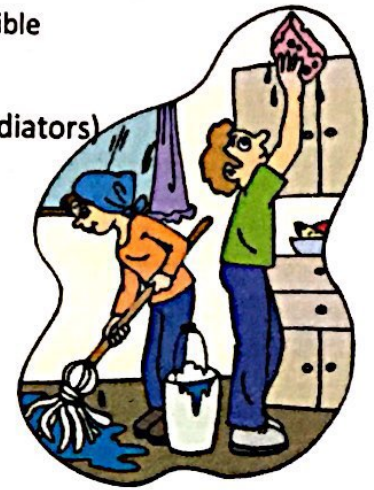
DRAFT

Fate (outcomes) of Acute inflammation

- **Resolution** : if injury is limited, short duration & regeneration is possible

Termination of acute inf response

- Neutralization of mediators (degraded by inhibitory mediators)
- Death of neutrophils by apoptosis
- Cleaning by macrophage
- Lymphatic drainage
- Normalization of vascular permeability .



- **Fibrosis (scar)** (severe damage in stable and permanent cells)
- **Chronic inflammation**
- **Spread (Direct – Lymphatic – Blood)**

Morphological Types of Acute inflammation:

Determined by cause – severity – type of tissue

- **Suppurative (purulent)** : containing **Pus**
 - Localized: "fibrin network is formed" : **Furuncle – Abscess – Carbuncle**
 - Diffuse: "fibrin is destroyed" by certain bacteria (streptococcus hem.)
 - e.g. : **Cellulitis** (Skin) – **Phlegmonas** (diffuse Suppurative in mucosa)
- **Non suppurative: No Pus**
 - **Catarrhal** : mild type , affects mucosa – excess mucous secretion
 - **Serous** : Inflammation of serous sacs. Also is seen in Skin
 - Excess fluid secretion by serous sac, or excess fluid exudates from plasma
 - e.g. **viral Plurisy**, **pericardial effusion** , **Blisters of skin** , **herpes simplex**
 - **Fibrinous**: affects serous sacs, and Lung in **Lobar Pneumonia**
 - **Pseudomembranous** : severe type, affects mucosa – a pseudo membrane is formed
 - **Allergic** : Hypersensitivity (**urticaria**, **asthma**) – **eosinophils** in tissue and blood

زى الافراج ديس
ليقة م. ا. م. م.
opening
علتاء الابد
طحييت
فبيطلاح
من صحت
الشعر

زيادة في الـ permeability

ببرسب ماء و فيبره لفل ال انا

hemorrhagic pneumonia

labor

phlebotomy

- **Necrotising** : severe necrosis by bacteria – e.g. **Vincent's angina**
- **Hemorrhagic** : severe type associated with vascular damage – e.g. **hemorrhagic pneumonia**

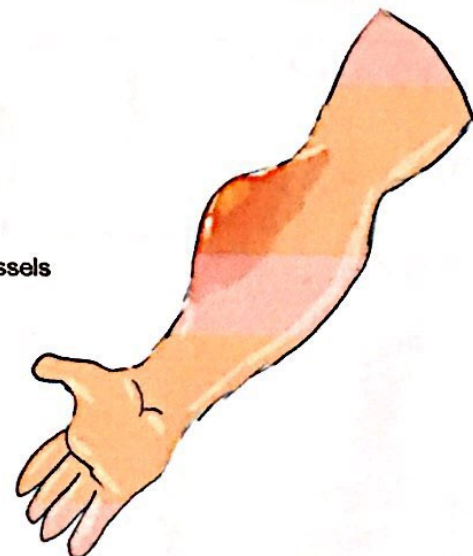
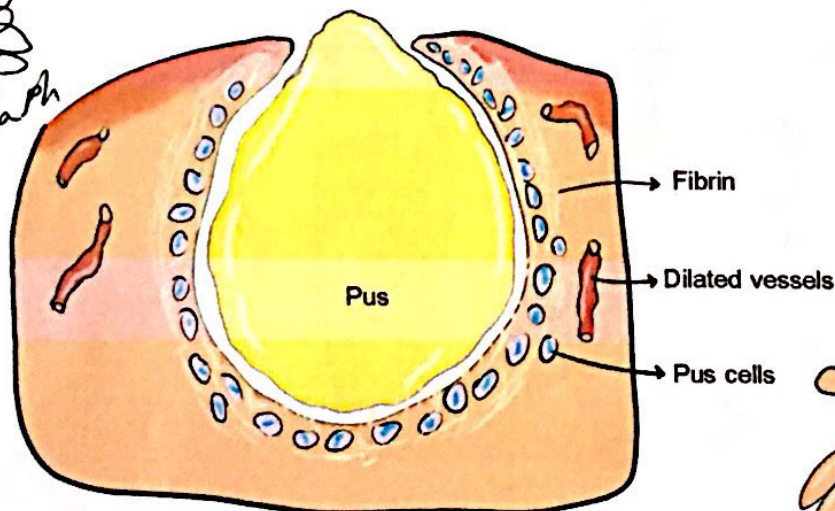
Suppurative inflammation

Pathogenesis of suppurative inflammation (pus formation):

- **Pyogenic bacteria** → They lead to tissue necrosis
- **Neutrophil aggregation** → phagocytosis of bacteria → death of neutrophils → pus cells
- **Pus cells** → release proteolytic enzymes on necrotic tissue → tissue liquefaction
- **Liquefied tissue** → attract more fluid exudate
 - **Composition of Pus**: liquefied necrotic tissue – neutrophils & pus cells – bacteria – fluid – damaged fibrin-RBCs

Pathogenesis of Localized suppurative inflammation (e.g. **Abscess**):

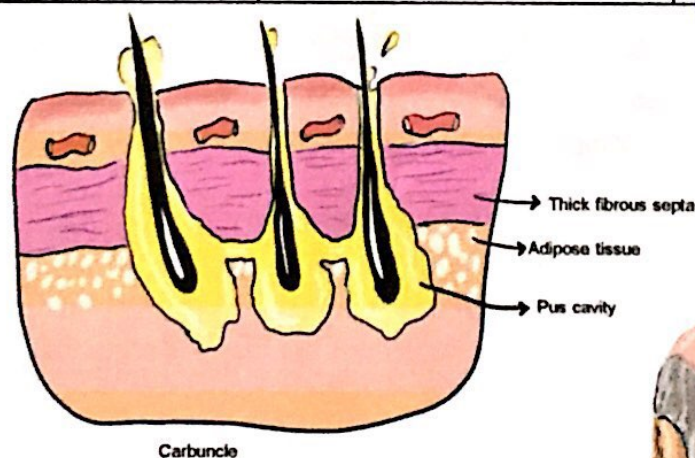
- The necrotic tissue is surrounded by neutrophils and pus cells
- The zone of necrotic tissue is liquefied from outside to inside → complete liquefaction
- The stph. Bacteria secrete **coagulase** → helps deposition of **fibrin** around pus
- 3 zones are seen now → zone of liquefied tissue – surrounded by zone of pus cells – surrounded by **Pyogenic membrane** (**pyogenic membrane** = pus cells + zone of fibrin + dilated vessels)
- Pain is due to severe tension in the cavity
- Abscess open by:
 - Superficial abscess → skin necrosis → pus escapes
 - deep abscess → may form Sinus
 - Renal abscess → open into calyces & renal pelvis → pyurea



Pathogenesis of diffuse suppurative inflammation (e.g. Cellulitis):

- The streptococcus hemolyticus secrete (*Hyalourinidase*) → dissolve tissue matrix
- It also secretes *Fibrinolysin*, *streptokinase* → damage fibrin
- Rapid and diffuse spread of bacteria (no localization)

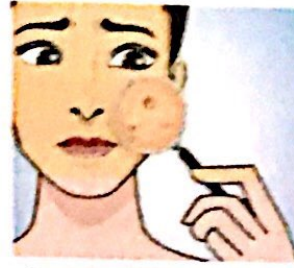
	Abscess	Carbuncle	Cellulitis
Type	Acute localized suppurative	Acute localized suppurative	Diffuse suppurative
Aetiology	(staph)	(staph) low immunity (D.M)	Strept
Mechanism	Coagulase → fibrin deposition	Coagulase → fibrin deposition	Fibrinolysin, Hyalourinidase → spread
Sites	-Skin -Organs	Tough skin with fibrous septa (Back of the neck, scalp, buttocks)	Loose areolar connective tissue (Face, limbs)
Morphology	• Irregular cavity • Surrounded by Pyogenic membrane 	• Multiple cavities • Separated by septa • Multiple openings 	• Diffuse red swelling • Inflamed lymphatics (red streaks) 
Pus	• Thick • Yellow	The same	• Less pus • Yellowish red (sanguinous)



Fast spread
of bacteria
الانتشار السريع
للبكتيريا

Furuncle (acne), (boil):

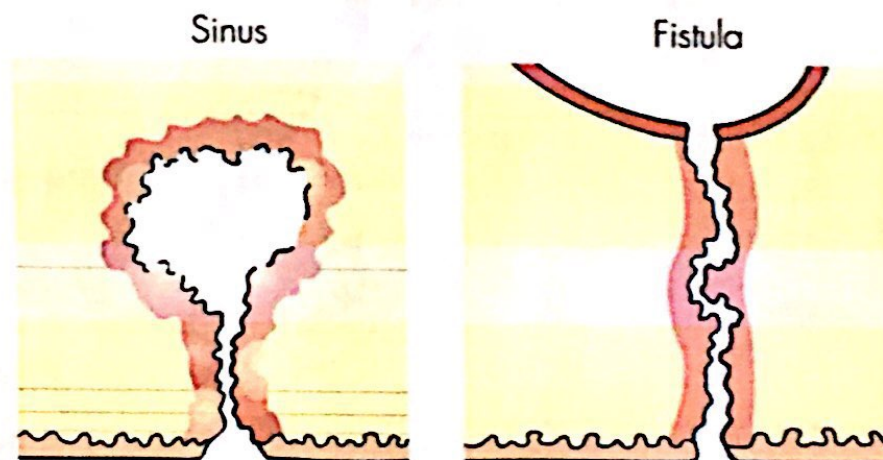
- Similar to abscess, but smaller and occur in hair follicles mainly in the face in males, Axilla in females.
- Infection is enhanced by obstruction of sebaceous gland by keratin and excess sebum → bacteria multiply → pus

Complications of abscess:

- Chronic (if not drained)
- Spread : Lymphatic (lymphangitis & lymphadenitis) , Blood (bacteremia, toxemia, septicemia, pyemia)
- Complications of healing:

- Ulcer (loss of surface epithelium)
- Sinus (tract of GT with single opening)
- Fistula (tract of GT with 2 openings)

N.B. Some fistulas are congenital (thyroglossal) , some are inflammatory (appendicular) , and others are neoplastic (recto-vaginal in cancer colon)



A sinus is a connection between a cavity lined with granulation tissue and an epithelial surface.

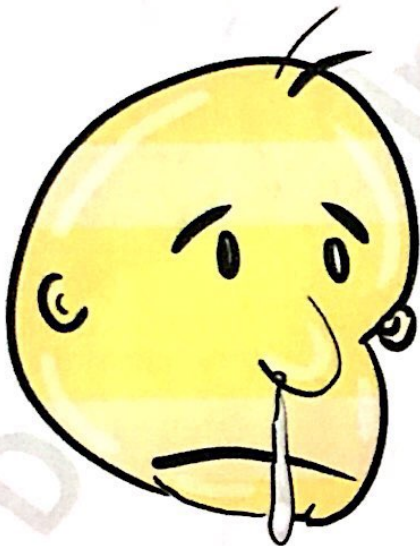
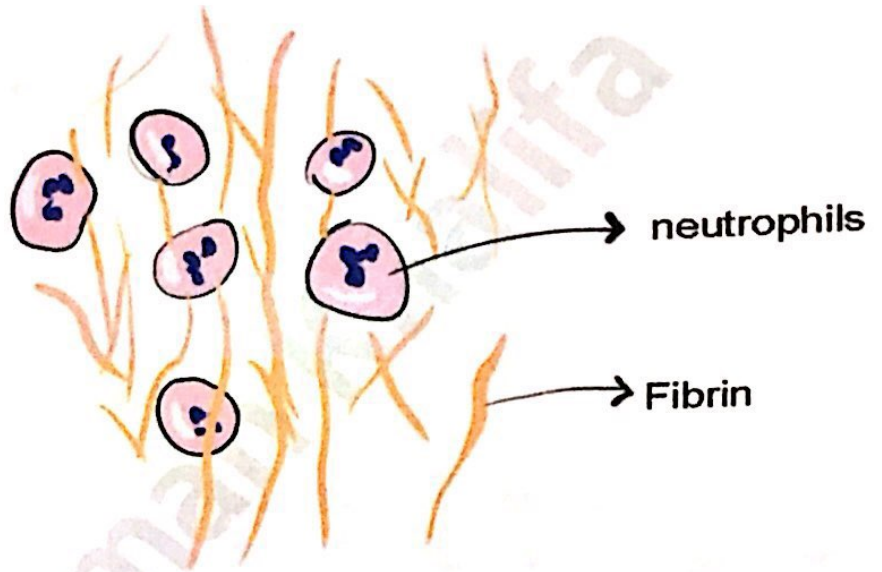
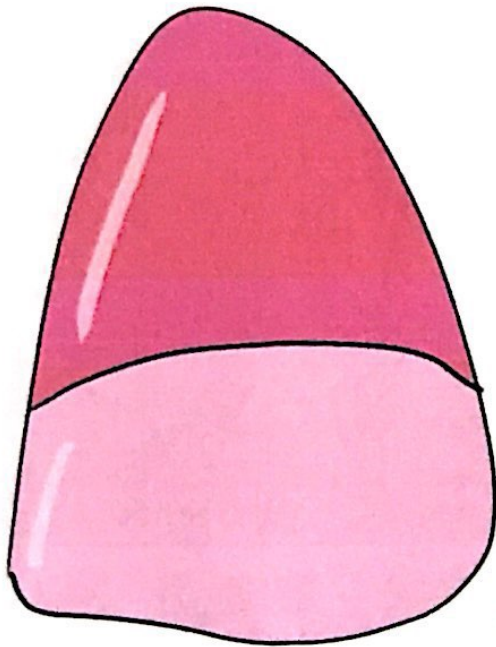
A fistula is a connection between two epithelial-lined surfaces.

Non Suppurative inflammation

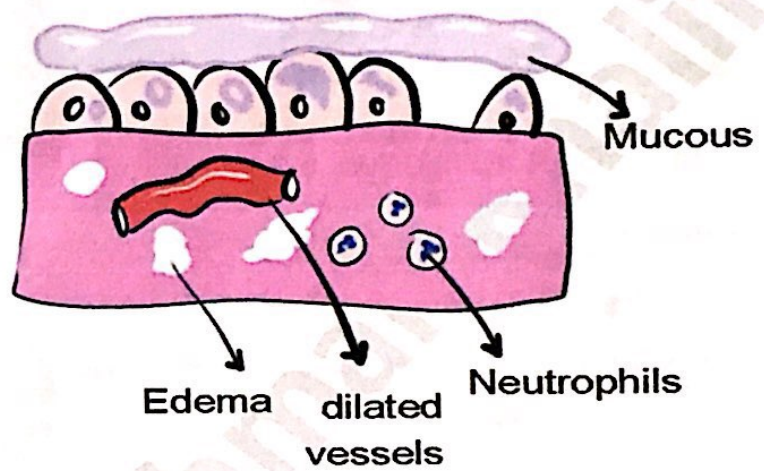
	Catarrhal	Fibrinous	Membranous
Sites	Mucosa e.g. nasal, bronchial, intestinal...etc.	- Serous sacs - Lung (lobar pneumonia)	- Larynx (diphtheria) - Colon (bacillary dysentery)
Pathogenesis	Injury of mucosa → excess mucous secretion	Severe injury → excess permeability to fibrinogen	-Bacteria on the surface → exotoxin → patchy necrosis -inflammation → fibrin & inflammatory cells → mixed with necrotic tissue -Toxemia
Gross	Red, swollen, hot, dry Thin secretion → then thick mucous secretion May become yellow	- Fibrin between parietal & visceral layers → opacity 'Bread and butter'	Thick, dirty white, adherent membrane detachment → bloody ulcers
Microscopic	<u>Mucosa:</u> <u>muroid degeneration,</u> <u>submucosa:</u> <u>vascular dilatation,</u> <u>edema</u> <u>and neutrophils</u>	<u>Amorphous or meshwork</u> <u>Eosinophilic</u>	<u>Membrane:</u> formed of <u>necrotic cells</u> <u>inflammatory cells & RBCs,</u> <u>fibrin</u> <u>and bacteria</u>
Fate	1-Resolution 2-mucoPurulent (infected)	1-Resolution (fibrinolysis & drainage) 2-Organization (activation of fibroblasts & capillaries) → scar → adhesions	Toxemia ↓ respiratory paralysis

fibrinogen → Fibrin
 Fibrin → Fibrosis
 11 Fibrosis
 2019

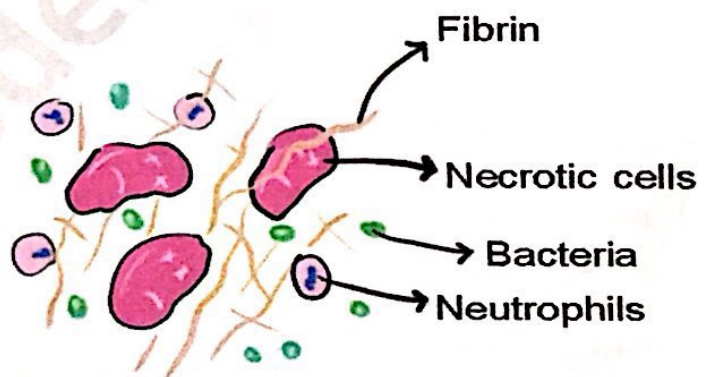
Fibrinous inflammation



Catarrhal inflammation



Membranous inflammation



	Acute inflammation	Chronic inflammation
Onset	sudden	
Duration	short	gradual
Causes	Enumerate ?	long Following acute Repeated acute attacks Chronic denovo : - Persistent infection - Persistent toxic agent - Autoimmune
Gross	<i>vascular</i> Prominent local signs	less
Microscopic	Blood vessels: dilated	Fibrous proliferation of <u>intima</u> (end arteritis obliterans) <i>تلف في جدار الشرايين</i>
	Fluid and fibrin: more	less
	Cells: <u>excess neutrophils</u> , macrophages	Excess mononuclear cells <u>lymphocytes</u> , <u>plasma cell</u> , <u>macrophages</u> And <u>giant cells</u> in some cases <i>→ chronic active</i> (neutrophils could be seen if there is persistent pyogenic infection or necrotic tissue)
	Fibrosis: absent	Proliferated granulation tissue & fibrosis
Organ changes	degeneration	Necrosis & fibrosis Systemic amyloidosis <i>يترسب في كل مكان في الجسم</i>
Fate	enumerate	Fibrosis
Types	Suppurative: contains pus Non suppurative: without pus	Specific: contains granuloma Non specific: without granuloma

Cells of chronic inflammation

Lymphocytes	-B-cell → Ig -T-cell → Lymphokines and react with macrophage
Plasma cell	Ig secretion (Antibodies)
Eosinophil	-Anti-parasitic (major basic protein MBP) → killing parasite and tissue necrosis -Role in Allergy is not clear
Mast cells & Basophil	Secrete Histamin
Macrophage	-interact with lymphocytes -Phagocytosis -secrete mediators & CK & G.F. for repair -Activated by (IF gamma) → Epithelioid cell → giant cell

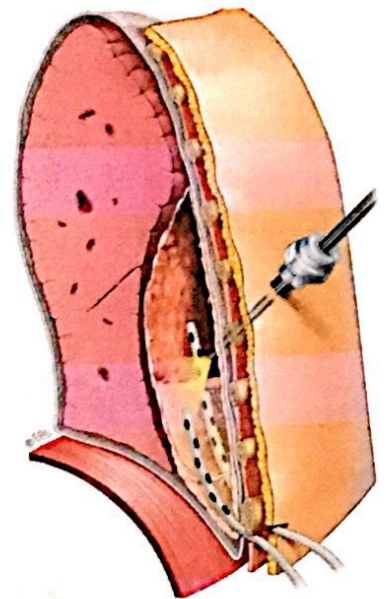
antiparasitic function

Empyema: pus accumulation in a hollow organ e.g.: gall bladder, pleura .

Ulcer: Local defect of skin or mucosal surface due to necrosis and shedding of epithelium.

Sinus: It is an abnormal tract lined by septic granulation tissue connecting a cavity to the outside .it has a blind end.

Fistula: it is an abnormal tract lined by septic granulation tissue connecting 2 cavities or between a hollow viscera and the surface. It differs from sinus as it is opened from both ends.



Bacteremia

Definition: Transient circulation of small amount of bacteria in blood

Causes: Spread from **septic focus** , **Tooth** extraction

Effects: **No** pathological effect (could be detected by blood culture)

Toxemia

Definition: circulation of **bacterial toxins** with pathological outcome

Causes:

- **Exotoxins** : secreted by bacteria (commonly gram +ve), e.g. **diphtheria**, strept.
- **Endotoxins** : damaged bacteria (commonly gram -ve), e.g. typhoid salmonella

Types:

- **Acute:** high amount of toxins, in severe infections
- **Chronic:** few amount of toxins in chronic infections (TB)

Pathological effects:

- **Acute (N C A D D)**
 - **Necrosis** of : **adrenal cortex**(fatal), focal hepatic, Acute tubular necrosis
 - **Constitutional symptoms** **FAHM** (Fever, Anorexia, Headache, Malaise)
 - **Acute heart failure** (due to **toxic myocarditis**) + Hype tension
 - **Degeneration** of parenchymatous organs (**hydropic/fatty**)
 - **DIC & septic shock**
- **Chronic (A A)**
 - **Anemia** & weight loss
 - **Amyloidosis**

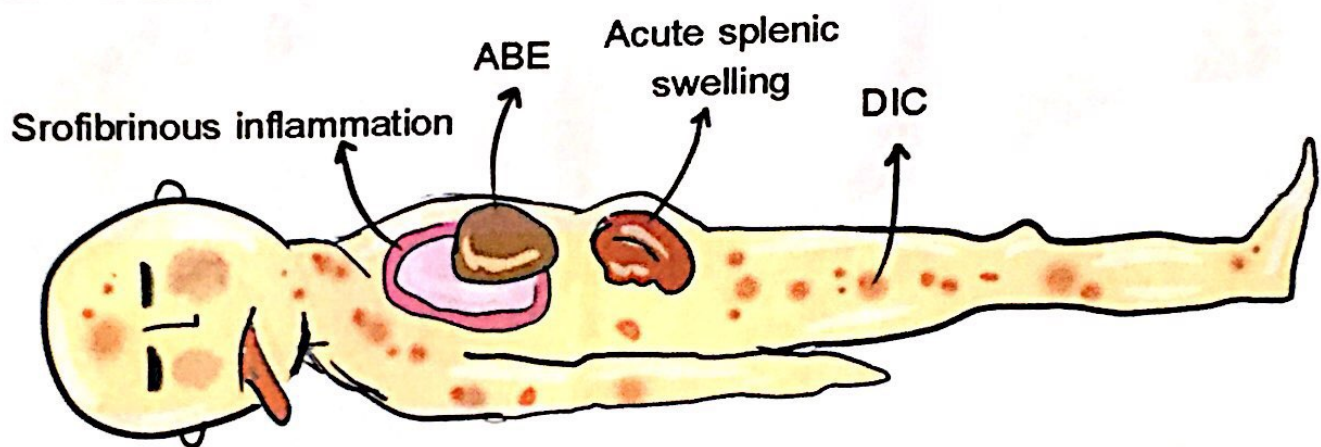
Septicemia

Definition: circulation and multiplication of bacteria and their toxins in blood

Causes: Pyogenic infection + low immunity

Pathological effects: are seen **post mortem**

- **Hemorrhage** (Due to DIC) → Appear in skin (*petichea*)
- **Heart Failure** (**ABE** → Acute heart failure) ⇒ *endocarditis*
- **Serofibrinous inflammation** in serous sacs (pericardial & pleural)
- **Acute Splenic swelling**
gross: Enlarged, *soft friable* (semi fluid)
micro: dilated sinusoids contain inflammatory cells – Atrophic follicles
- **Effects of Toxemia (NCAD D) mainly Adrenal necrosis and hemorrhage**



Septicemia

Pyemia

Definition: Formation of multiple pyemic abscesses or septic infarctions due to impaction of septic emboli.

Types:

- **Systemic:** septic emboli carried by systemic circulation
 - Suppurative otitis media
 - Lung abscess (septic emboli in infected pulmonary veins)
 - ABE of left side
 - Purperal sepsis
 - Acute hematogenous osteomyelitis
- **Portal:** systemic emboli from GIT (Suppurative cholecystitis, suppurative appendicitis, Colon suppuration, infected pile) → septic emboli through portal vein → pyemic abscesses in liver

Pathogenesis:

septic thrombo-phlebitis → fragmentation of septic thrombi by proteolytic enzymes → detachment → spread of multiple fragments → impaction inside small vessels of distant organ → pus formation around vessels → multiple abscesses

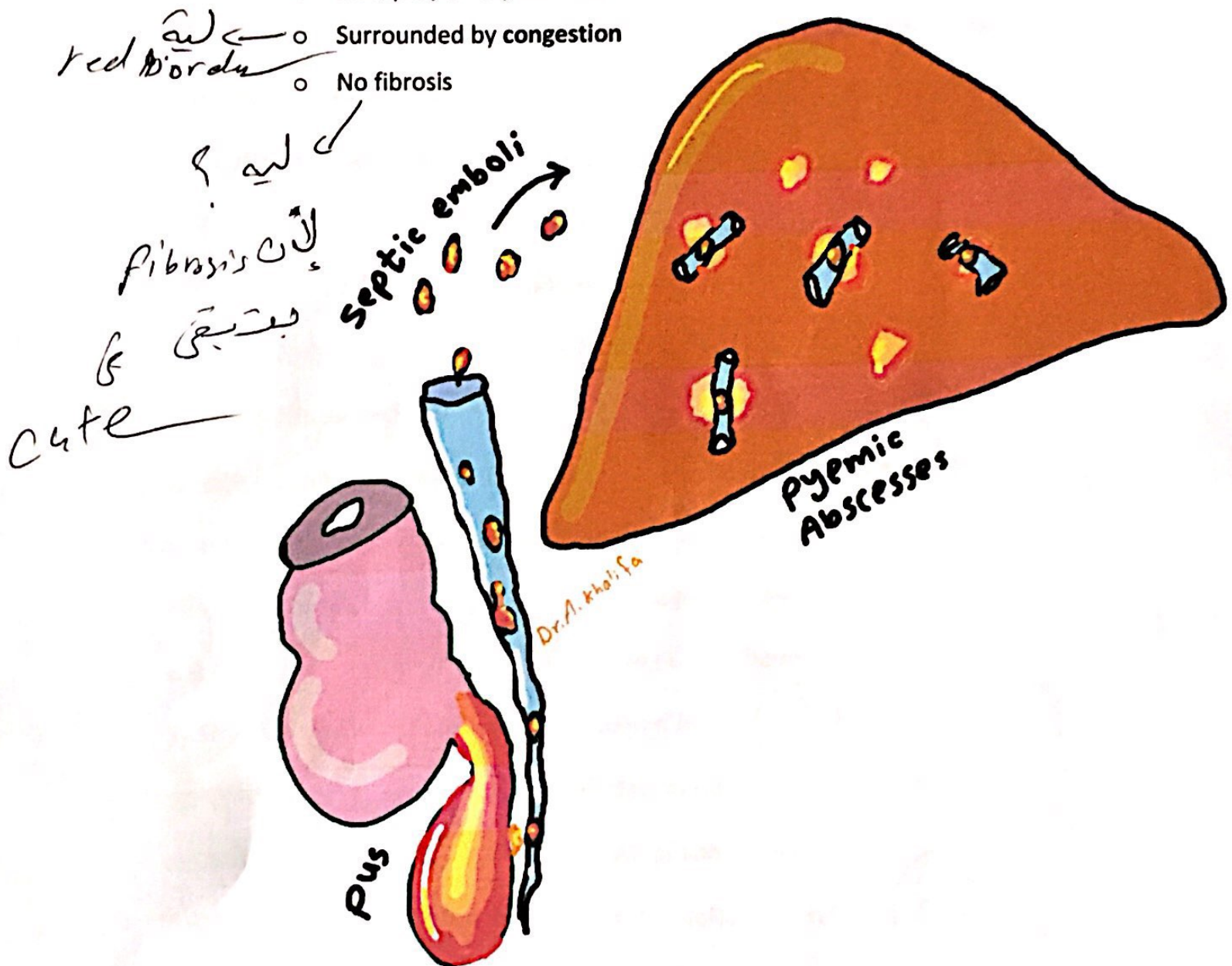
Pathological effects:

- Abscesses in distant organs (commonly lung, liver)

- Multiple, Small, Rounded

- Surrounded by congestion

- No fibrosis



فسي في مكان
thrombus
emboli
تلقه

MCQ

1-Swelling in Acute inflammation is induced by: (b)

- a) Vascular dilatation
- b) Inflammatory exudate
- c) Cellular proliferation
- d) bacterial proliferation

2-Which of the following events is responsible for increased permeability: (a)

- a) Endothelial cell contraction
- b) Vascular constriction
- c) Increased arterial blood pressure
- d) All of the above

3-Localization of Acute inflammation is induced by: (b)

- a) Fibrosis
- b) Fibrin
- c) Non
- d) All of the above

4-All the following are True about Fluid exudate EXCEPT: (d)

- a) Rich in Fibrinogen
- b) Turbid
- c) High specific gravity > 1020
- d) Drained by venules

5-Rolling of Leukocytes on endothelial surface requires: (a)

- a) Selectin family
- b) Integrin family
- c) ICAM
- d) All of the above

6- Stable adhesion of leukocytes is helped by: (d)

- a) VCAM
- b) Integrin family
- c) ICAM
- d) All of the above

7- Phagocytosis takes place by which of the following cells: (d)

- a) PMNLs
- b) Monocytes
- c) Histocytes
- d) All of the above

8- Which of the following mediator is the major mediator of pain: (a)

- a) Pg E2
- b) Histamin
- c) Leukotreins
- d) Major basic protein

9- PMNLs reach the site of inflammation within:

- a) 6-24 hours
- b) 2-3 days
- c) 5 days
- d) one week

10- The following example represents Fibrinous inflammation:

- a) Diphtheria
- b) Empyema
- c) Lobar pneumonia
- d) Scar formation

11- Marked inflammatory edema could be seen in the following sites EXCEPT:

- a) Pericardium
- b) Skin
- c) Alveoli
- d) Bone

12- Numerous eosinophils are found in:

- a) Lung abscess
- b) Suppurative appendicitis
- c) Allergic rhinitis
- d) none of the above

13- Diphtheria is an example of:

- a) Allergic inflammation
- b) Chronic inflammation
- c) Acute non suppurative
- d) none of the above

14- Localization of acute abscess is helped by:

- a) Polymorphs
- b) Bacterial coagulase enzymes
- c) Bacterial fibrinolysin
- d) Proteolytic enzymes of pus cells

15- Acute abscess is lined by:

- a) Fibrous tissue
- b) Pyogenic membrane
- c) Proliferated epithelial cells
- d) All of the above

16- All about cellulitis are true EXCEPT:

- a) Occurs in skin
- b) Caused by streptococci
- c) Large amount of pus in a cavity
- d) Fibrinolysin is essential for pathogenesis

17- Phagocytosis is activated by:

- a) Opsonin
- b) Cytokines
- c) Serotonin
- d) Lysosomal enzymes

18- Histamine is the direct cause of:

- a) Phagocytosis
- b) Leukocytosis
- c) Emigration
- d) Vascular permeability

19- The following substance is a positive chemotactic of neutrophils:

- a) C5a
- b) C3a
- c) Both a & b
- d) none

20- A typical chronic inflammatory reaction is characterized by:

- a) Lymphocytes & plasma cells
- b) Macrophage & occasionally eosinophils
- c) Fibrosis
- d) All of the above

21- Which of the following cells is the most pathognomonic for chronic inflammation:

- a) Lymphocytes
- b) Macrophage
- c) plasma cells
- d) eosinophils

Inflammation

- 1) Which of the following is a potent chemotactic factor:
 - a) TNF
 - b) Prostaglandin
 - c) Interleukin-8
 - d) Complement c3b
- 2) A patient presented with a red swelling on the back of the neck with multiple loculi discharging pus, which type of inflammation is this?
 - a) Localized suppurative inflammation
 - b) Pseudomembranous inflammation
 - c) Fibrinous inflammation
 - d) Diffuse suppurative inflammation
- 3) General features of chronic inflammation include all Except:
 - a) Tissue necrosis
 - b) Chronic inflammatory cells
 - c) Blood vessels are thin walled, dilated
 - d) Fibrosis
- 4) A blood sample did not show bacteria but on performing a blood culture bacteria were detected. This is:
 - a) Pyemia
 - b) Septicemia
 - c) Toxemia
 - d) Bacteremia
- 5) Amyloidosis is one of the complication that can follow
 - a) Acute toxemia
 - b) Chronic toxemia
 - c) Septicemia
 - d) Pyemia
- 6) Examples of chronic specific inflammation:
 - a) Bilharziasis
 - b) Tuberculosis
 - c) Chronic osteomyelitis
 - d) A&B
- 7) ESR is elevated in:
 - a) Acute inflammation
 - b) Chronic inflammation
 - c) A & B
 - d) None of the above
- 8) A 7 year old girl presented with fever, chills, severe abdominal pain and dysentery. Endoscopic examination showed that the colon was

markedly swollen and red with few areas showing loosely adherent thin grayish white membrane. All of the following complication can occur EXCEPT:

- a) Acute renal failure
 - b) Acute heart failure
 - c) Acute adrenal insufficiency
 - d) Amyloidosis
 - e) Acute toxemia
- 9) A 20 year old male with painful urination, urine cytology revealed many neutrophils. Release of which of the following chemical mediators is most likely to drive neutrophils towards the organism?
- a) ROS
 - b) Complement C5a
 - c) Histamine
 - d) Bradykinin
- 10) During autopsy, for a 65 year old male multiple tiny yellowish nodules were found surrounded by congestion in the lung, which of the following could be related to these nodules:
- a) Acute cholecystitis
 - b) Suppurative appendicitis
 - c) Suppurative tonsillitis
 - d) Infected pills
- 11) In the cellular event of the acute inflammatory response, weak and transient(rolling) leukocytic adhesion to the endothelial cells are mediated by:
- a) Integrins
 - b) TNF
 - c) Selectin family
 - d) IL-1
- 12) Which of the following inflammatory cells predominate in parasitic infestation:
- a) Lymphocytes
 - b) Eosinophils
 - c) Plasma cells
 - d) Histiocytes
- 13) Chemotaxis is:
- a) Adhesion of leukocytes to the endothelial cells
 - b) Ingestion of bacteria by leukocytes
 - c) Attraction of leukocytes to the site of inflammation
 - d) Facilitation of attachment of bacteria to leukocytes

- 14) A patient presented with pain of his knee and the doctor suspected acute inflammation, all of the following are expected to be elevated in the blood Except:
- a) Albumin
 - b) C reactive protein
 - c) Amyloid associated protein
 - d) Fibrinogen
- 15) Acute lobar pneumonia is an example of:
- a) Serious inflammation
 - b) Suppurative inflammation
 - c) Fibrinous inflammation
 - d) Pseudomembranous inflammation
 - e) Allergic inflammation
- 16) Lobar pneumonia is an example of:
- a) Chronic nonspecific inflammation
 - b) Non suppurative inflammation
 - c) Diffuse suppurative inflammation
 - d) Localized suppurative inflammation
 - e) Chronic specific inflammation
- 17) Which of the following is the most important mediator in the last event in phagocytosis:
- a) Reactive nitrogen species
 - b) Selectins
 - c) Histamine
 - d) Prostaglandins
- 18) Acute inflammation is a prominent feature in:
- a) Bacillary dysentery
 - b) Autoimmune reactions
 - c) Sclerosis
 - d) Both A & B
 - e) Both B & c
- 19) In abscess formation, fibrin is responsible for:
- a) Pus formation
 - b) Increase the size of the abscess
 - c) Fistula formation
 - d) Localization of the infection
- 20) Recognition and attachment of leukocytes to most microorganisms facilitated by:
- a) C3b fragment of complement
 - b) Soluble bacterial products
 - c) Prostaglandin
 - d) Bradykinin

- 21) Bacillary dysentery is usually associated with:
- a) Septicemia
 - b) Acute toxemia
 - c) Chronic toxemia
 - d) Bacteremia
- 22) A 5 year old girl had a fever of 3 days duration. On physical examination, she has red swollen tonsils with yellow spots. Swab from the spots obtained yellowish fluid. Which type of cell is most likely to be numerous in the fluid?
- a) Plasma cell
 - b) Macrophages
 - c) Fibroblasts
 - d) Dead and living polymorph nuclear leukocytes
- 23) A 40 year old woman complained of patchy lesion in the skin causing itching. A biopsy revealed endarteritis obliterans, angiogenesis, fibrosis, with diffuse infiltration by lymphocytes and macrophages. Which of the following terms best describe this process?
- a) Acute inflammation
 - b) Granulomatous inflammation
 - c) Chronic inflammation
 - d) Suppurative inflammation
 - e) Serofibrinous inflammation
- 24) Disseminated intravascular coagulopathy is a complication of:
- a) Septicemia
 - b) Chronic toxemia
 - c) Bacteremia
 - d) Pyemia
- 25) These are character of pyemic abscesses except:
- a) Multiple
 - b) Small
 - c) Surrounded by fibrosis
 - d) Nearly same size
- 26) Which of the following is responsible for fever that develops with the acute inflammation:
- a) TNF, IL1, prostaglandins
 - b) Interleukin-8
 - c) Histamine
 - d) Leukotrienes

27) A 15 year old boy complaining of marked ill-defined erythema and edema in his eyelid. CT showed extension of this process into connective tissue of the orbit. The most likely diagnosis of his condition:

- a) Carbuncle
- b) Cellulitis
- c) Abscess
- d) Phlegmonous inflammation
- e) Furuncle

Easy Pathology

Dr. Abdelrahman Khalifa

Chapter

Cell Injury

Ainshams 2018 - 2019

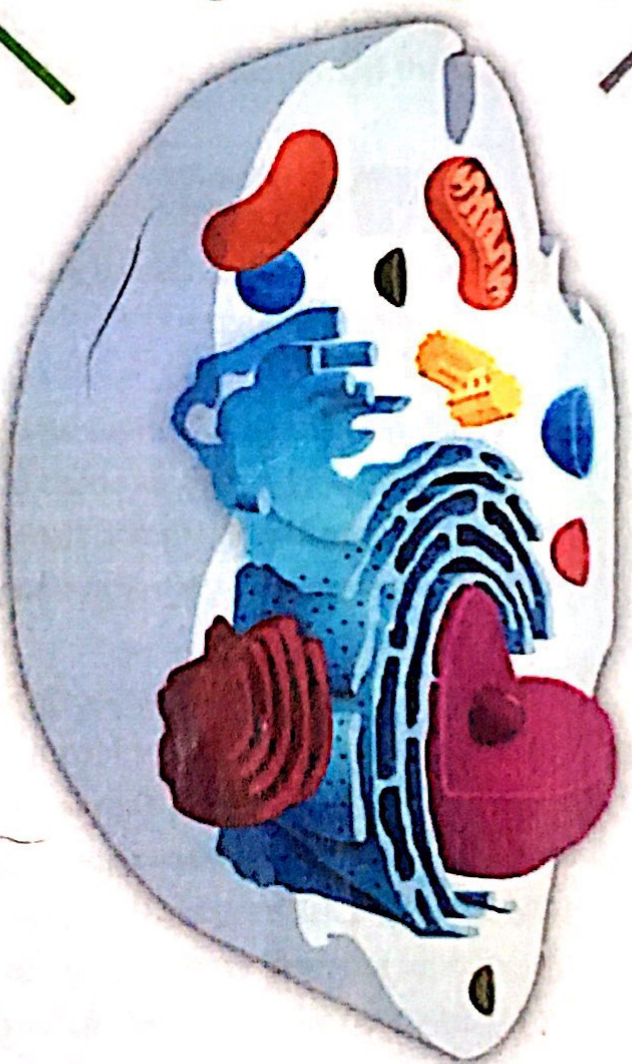
I. Cell response to injury

- 1** **Adaptation**
- 1- Atrophy
 - 2- Hypertrophy
 - 3- Hyperplasia
 - 4- Metaplasia

- 2** **Reversible**
- 1- Hydropic degeneration
 - 2- Hyalinosis

- 3** **Irreversible**
- 1- Necrosis
 - 2- Apoptosis
 - 3- Gangrene

- 4** **Accumulation & tissue**
- 1- Fatty change
 - 2- Melanin pigment
 - 3- Hemosiderin
 - 4- Pathological calcification
 - 5- Hemorrhage



II. Cell aging

Cell injury: Morphological & functional changes of cells following **stressful conditions**
 The Outcome of cell injury depends on : **Type of tissue - Type of injury**

- **Adaptations** (New steady state to maintain viability & function)
- **Reversible injury** (with mild/moderate injury, recover is possible)
- **Irreversible injury** (with severe persistent injury → cell death necrosis & apoptosis)
- **Accumulations & tissue deposits** (In some types of tissues, in certain situations, tissue cannot utilize certain types of substances that accumulate in tissue or cells)

Adaptation

Adaptations are almost reversible changes (except in **connective tissue metaplasia**). These changes occur in number, size, function, or type of cell. They are **physiological** to adapt hormonal or chemical changes. Or **Pathological** to adapt harmful situations.

N.B. Cell death may occur in some situations, if the injury is severe and persistent

1. Atrophy

Def:- Decreased size of organ due to decreased size and/or number of cells in well-formed organ or tissue

Physiological

- ex:-
- Lymphoid tissue in **thymus** after **puberty**
 - Lymphoid tissue, & **appendix** in old age
 - **Brain** & **Heart** atrophy in old age
 - Atrophy of **ovaries** after **menopause**

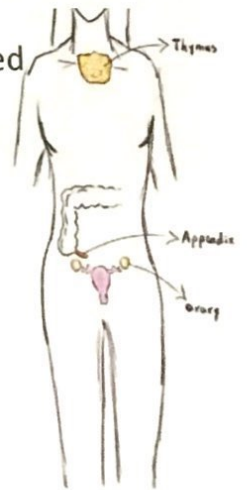
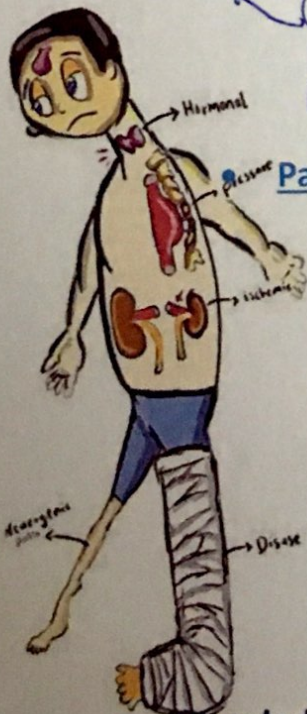
Pathological

- **Ischemic** atrophy (chronic ischemia) → tissue atrophy
- **Pressure** atrophy e.g. Aortic aneurism → atrophy of **vertebral bodies** (discs are spared) *Cartilage not atrophy because it's avascular.*
- **Neurogenic** e.g. wasting of muscle in motor neuron injury)
- **Disuse** atrophy (fractured limb → immobilization → muscle atrophy)
- **Hormonal** (e.g. Pituitary diseases with lack of TSH → thyroid atrophy)
- **Nutritional** protein deficiency (e.g. lack of protein in **marasmus** → muscle atrophy)

protein deficiency

Morphology:

Decreased cell **size** – decreased **organelles** (mitochondria, ER, myofilaments) – **autophagy** vacuoles (e.g. lipofuscin)





Aplasia :

Failure of organ development which remains rudimentary

Agenesis:

Failure of organ formation (complete absence)

N.B. In Apoptosis, number of cells is reduced , which may lead to organ atrophy

2.Hypertrophy

Increased size of organ due to increased size of cells
(Mostly in non-dividing permanent cells)

• Physiological

- **Pregnancy** → uterine smooth muscle hypertrophy
- **Exercise** → muscle hypertrophy

*mixed
Hypertrophy
and
Atrophy*

• Pathological

- Hypertension, valve diseases → **cardiac** hypertrophy
- **Pyloric** stenosis → gastric hypertrophy
- Compensatory in one **kidney** after nephrectomy of the other one.
- Urethral obstruction → **bladder** hypertrophy

*and
Hypertrophy*



Morphology: Increased cell size – Increased nuclear size

3.Hyperplasia

Increased size of organ due to increased number of cells

Site: Labile & stable cells (cells with mitotic ability), NOT in permanent cells

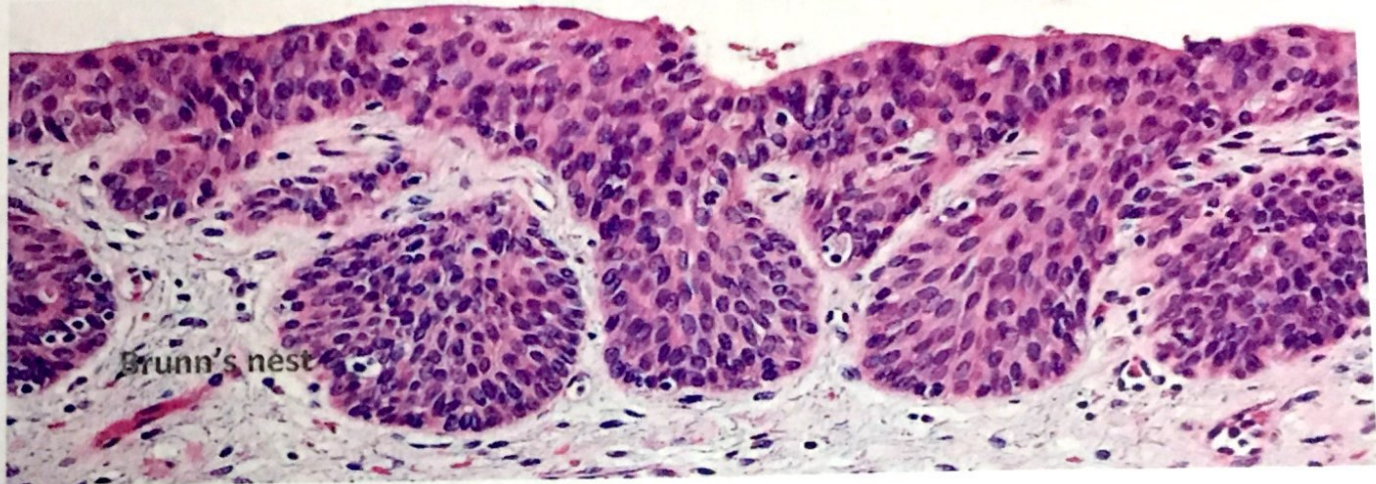
• Physiological

- Hormonal : **Breast** (during lactation) , **Uterine** muscle (pregnancy)
- Compensatory : e.g. **Liver** (partial hepatectomy) , **Kidney** (nephrectomy)



• Pathological

- Hormonal :
 - Mammary hyperplasia (fibrocystic disease)
 - Endometrial hyperplasia
 - Prostatic hyperplasia
 - Thyroid hyperplasia in Goiter (elevated TSH)
 - Bone marrow , following blood loss (erythropoietin)
- Reactive : L.N. hyperplasia following infection
- Chronic Irritation : urothelial hyperplasia in bilharziasis (Brunn's nest)



N.B. Hyperplasia may occur with hypertrophy in some cases (e.g. pregnant uterus)
It is precancerous in some pathological cases (endometrial, mammary)

	Hyperplasia	Neoplasia (Tumor)
Aetiology	Initiated by a cause (stimulus)	Multi-factorial
Course	Self-limited	Uncontrolled
Fate	-Reversible (after removal of the cause)	Irreversible

4. Metaplasia

Transformation of a cell into another type of differentiated cell within limits
mechanism: Abnormal stimuli (Irritant) → Reprogramming of stem cells → new type

• Epithelial metaplasia

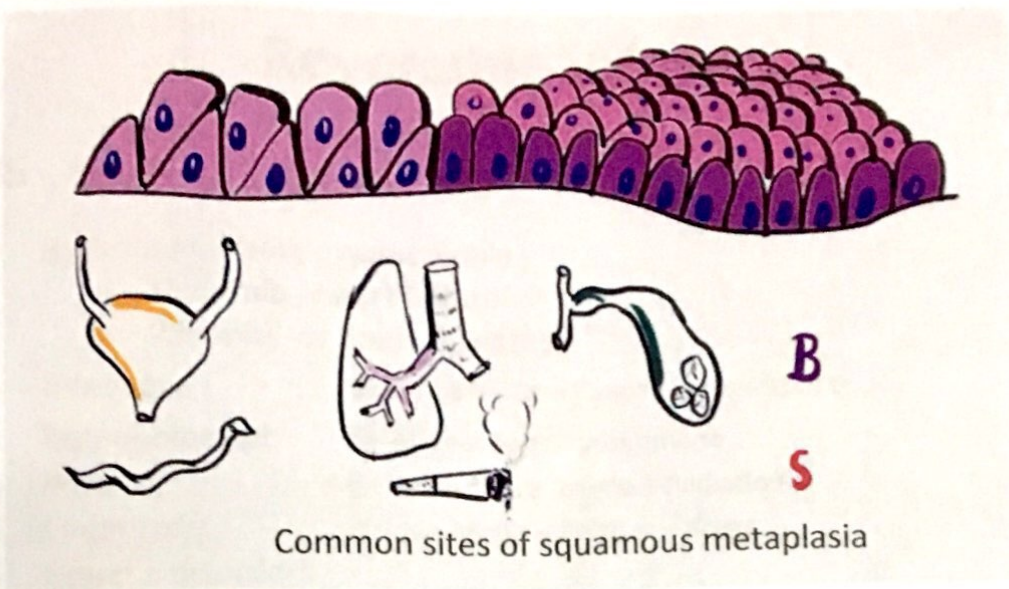
○ Squamous metaplasia

- Smoking → metaplasia of Bronchi in chronic bronchitis
- Shistozoma → metaplasia in urinary Bladder
- Stones → metaplasia of urinary bladder or gall Bladder
- In Chronic nasal polyp
- Endocervix in Chronic Cervicitis

Reversible

endo → clonary →
exo → squamous →
vagi

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Common sites of squamous metaplasia

o Columnar metaplasia

- Esophagus: Barrett's esophagitis in case of GERD
- Stomach: Intestinal metaplasia in Chronic gastritis
- Bladder: Cystitis cystic → cystitis glandularis

Gastro esophageal Reflux Disease

• Mesenchymal metaplasia

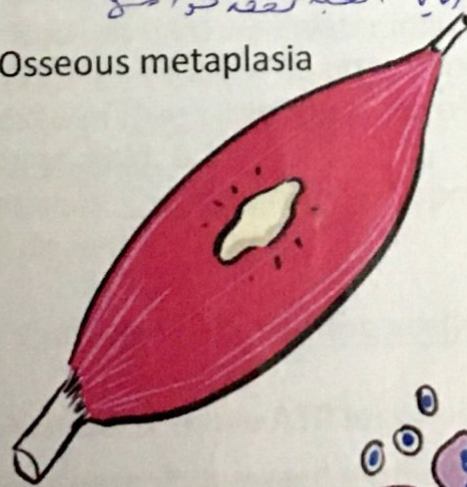
o Osseous

- Myositis ossification in muscle
- Ossification of calcified areas
- Ossification of tumor stroma

o Cartilagenous metaplasia of Splenic capsule (in splenomegaly)

o Myeloid metaplasia in case of blood loss (extramedullary hematopoiesis)

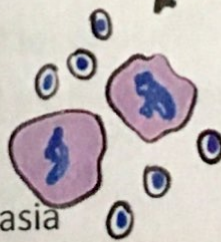
Osseous metaplasia



Cartilagenous metaplasia



Myeloid metaplasia



all types of metaplasia are pre cancer

Reversible injury

a ↓ Concentration inside the cell

Causes:

- Hypoxia (decrease oxygen supply)
 - Ischemia , heart failure
 - Anemia, or heart diseases
- **Infections** : viral – bacterial – fungal – parasitic ...etc.
- **Immunological**: Ag-Ab reaction, Autoimmune
- **Physical**: e.g. Temperature- trauma – Radiation
- **Chemicals**: Acids – Alkalis – Poisons – drugs
- **Genetic** disorders
- **Nutritional** : protein deficiency (marasmus, Kwashiorkor) – excess fat

Factors affecting response to injury:

Type of injury (severity & duration)

Type of cells (labile – stable – permanent)

Skeletal muscle resists hypoxia for 2-3 hours, Cardiac muscle resists for 20-30 minutes

Mechanism of cell injury



↓ ATP → Defective cell membrane transport (**Na-K pumps**) →
↑ intracellular Sodium (Na) → water influx → Cell Swelling & organelles swelling
mitochondria damage (appear as amorphous deposits or vacuoles) :

- Release of **free radicals** (Active oxygen metabolites) → damage of proteins, lipid, & DNA
- Release of **Cytochrome C** → apoptosis
- **ATP depletion**



↓ ATP → Calcium influx → ↑ **intracellular Ca** → **activate damaging enzymes**:

- ATPase → **more ATP loss**
- Protease → damaged proteins & nucleoprotein
- Caspase → Cell apoptosis
- Phospholipase →

▪ membranes damage: → Myline figures

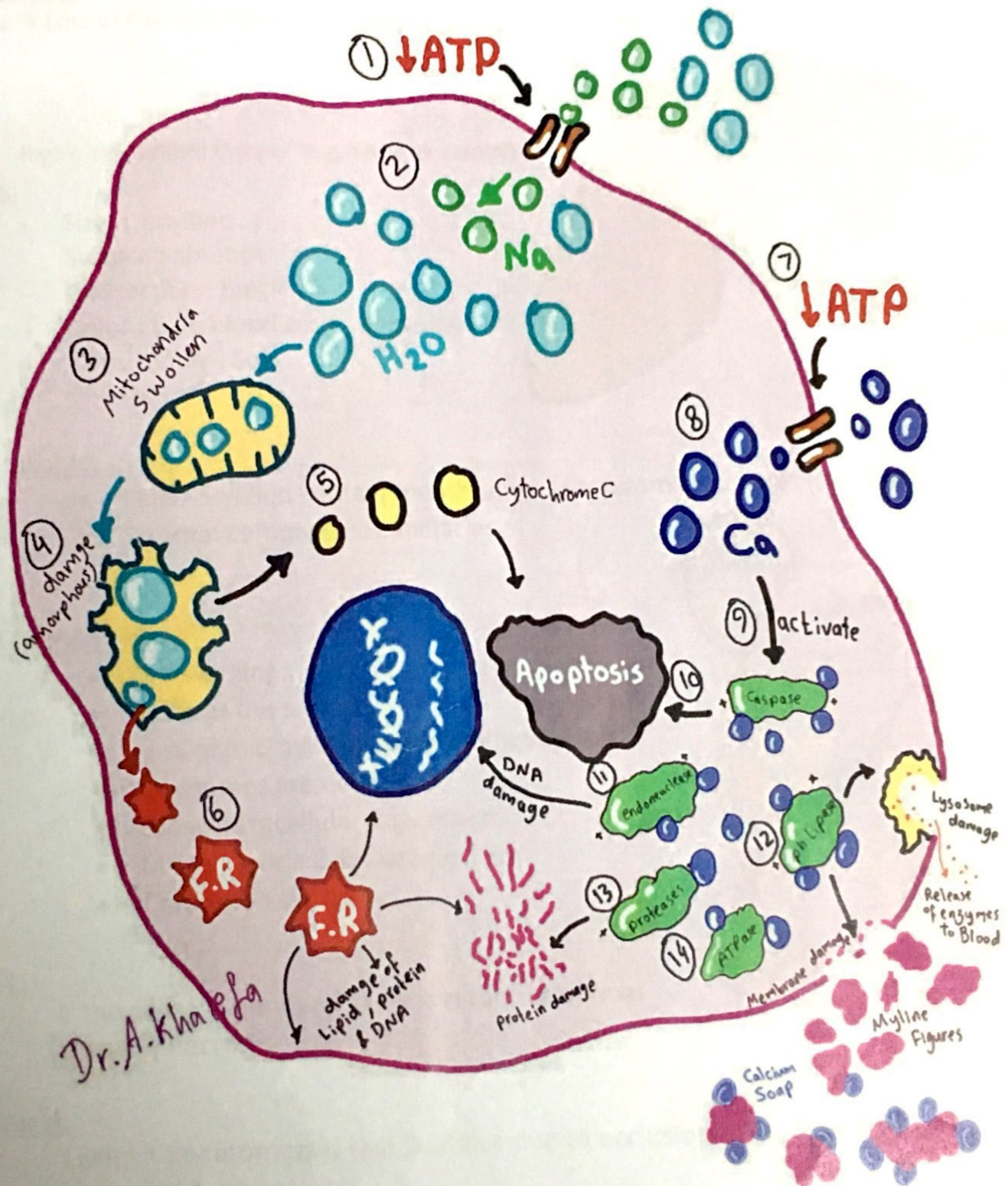
- Phagocytosed
- Bind with Ca → saponification
- Release of intracellular enzymes to blood
- Mitochondrial & lysosomal damage

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○ Endoneuclease → damage of nucleus, DNA, RNA

- Pyknosis(condensation)
- Karyorhexis(fragmented)
- Karyolysis (dissolution)

⚠️ ↓ ATP → Anaerobic glycolysis → lactic acidosis → activates enzymatic digestion



Points of no return: The critical phenomena that lead to irreversible changes are permanent **Mitochondrial dysfunction** & **cell membrane damage**.

Hydropic degeneration (cloudy swelling)

Definition: Reversible cell injury, with intracellular water vacuoles

Causes: causes of cell injury (enumerate), but mild for short duration

Pathogenesis:

Hypoxia → Loss of ATP → Failure of sodium pumps → Sodium & water influx → Cell swelling

Site: highly specialized organs (e.g. Liver, & kidney)

Gross:

- Size : swollen
- Surface : smooth
- Cut section : bulging
- Color : pale bloodless (compressed capillaries)
- Consistency : Soft

الزوجة

Microscopic:

- **Cells:** Swollen – intact membrane – cytoplasmic vacuoles (swollen ER)
- **Stroma:** compressed capillaries

E/M (ultrastructure):

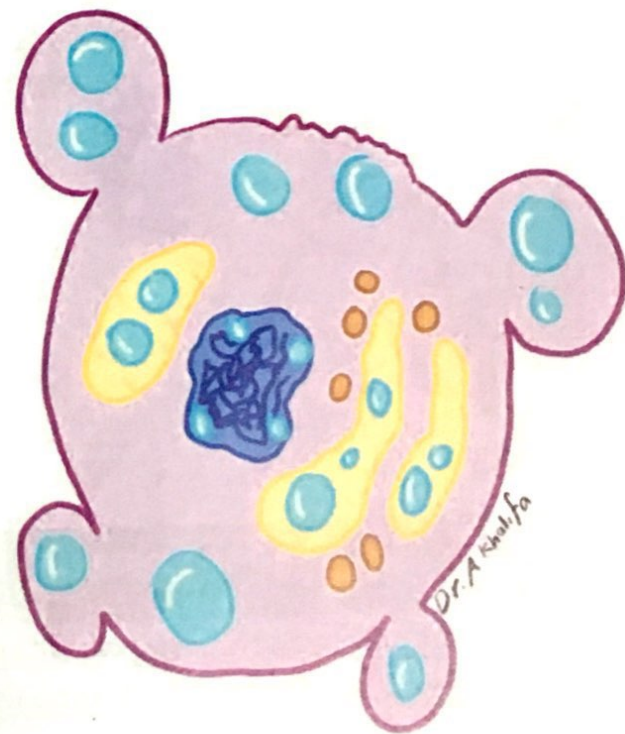
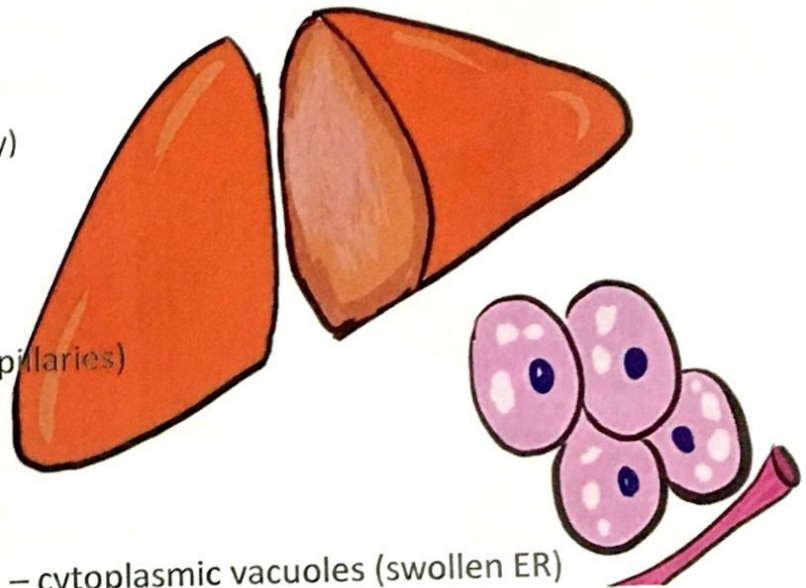
- Cell swelling
- Blebs at the surface
- Loss of microvilli in some epithelial cells
- Ribosomes are detached
- Loose intracellular attachment
- Mitochondria & ER are swollen
- Chromatin clumping

Fate:

If the cause is removed → cells return to normal
If not → necrosis

Clinical:

Liver → hepatomegaly and jaundice due to occlusion of bile canaliculi
Intestine → diarrhea



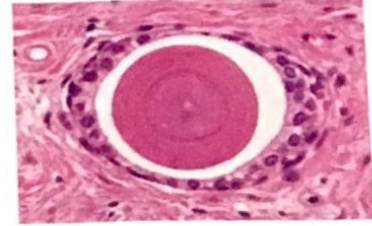
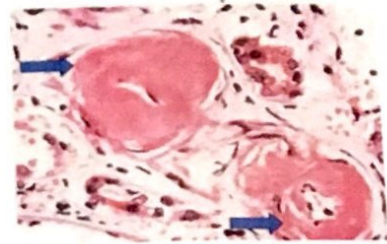
Hyalinosis

Microscopic change in tissue **proteins**, which became **glassy**, **homogenous** & **eosinophilic**.

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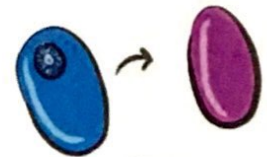
1. Extracellular hyalinosis (CAPS)

1. **Chronic Glomerulonephritis** : hyalinosis of glomeruli
2. **Arteriolosclerosis** : in benign hypertension
3. **Prostate: Corpora amylacea** in prostatic hyperplasia
4. **Scar** : hyalinosis of collagen in old scar



2. Intracellular hyalinosis: (4 P)

- **Plasma cell** → accumulated Ig → **Russel body**
- **Parenchyma of liver** (in alcoholism) → alteration of intermediate filaments → **Mallory body**
- **Proximal convoluted tubules** (in proteinurea) → reabsorption of protein → **Hyaline bodies**
- **Pneumonia, or Diphteria** : → Toxemia → **Abdominal muscle injury** → **Lactic acidosis** → hyaline change of muscle proteins → homogenous pink & **loss of striations** → **(Zenker's degeneration)**



Mucoid changes	Myxoid changes
Intracellular Accumulation of mucinous material (glycoprotein) in epithelial cells	Extracellular Accumulation of mucinous material (glycoprotein) in connective tissue
Catarrhal inflammation Mucoid Carcinoma Muco-Cele	Myxoid changes in tumors Myxoedema

NECROSIS

Definition: Death of **group of cells** inside living tissue, directly, or following degeneration. Necrosis is surrounded by inflammation.

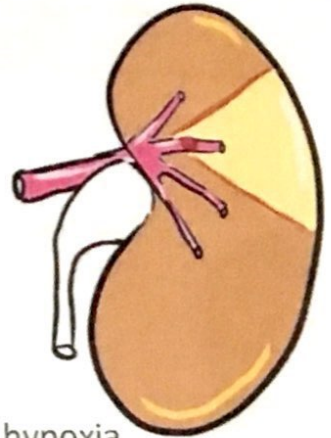
Pathological picture:

- **Cytoplasm:** **eosinophilia** (due to loss of RNA & denaturated proteins)
- **Nucleus:** Pyknosis – Karyorhexis – Karyolysis

Morphological Types:

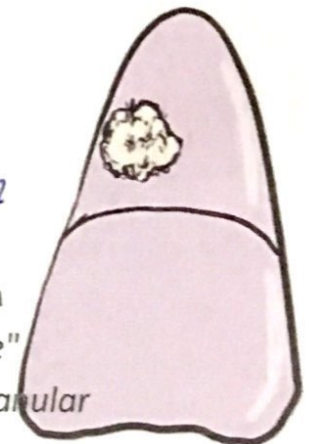
Coagulative necrosis:

- The most common type of necrosis
- Tissue resembles "Boiled meat"
- **Cause:** Hypoxia is the most common, mainly ischemia
- **Gross:** dead area is "firm", and "pale"
- **Microscopic:** Cellular details are lost
- **architecture is preserved** in early stage (Fibrous stroma resists hypoxia, but later, inflammatory cells lead to lysis of architecture)
- e.g.: Myocardial infarction (MI), Renal infarction



Caseation necrosis:

- Tissue resembles Casine "**Cheese**"
- occur in Tuberculosis (T.B.)
- **Cause:** Hypersensitivity against T.B. bacteria → tissue caseation
- **Gross:** dead area is "soft cheesy, granular", and "yellowish white"
- **Microscopic:** tissue became **structureless homogenous**, with granular areas + **granuloma of TB**

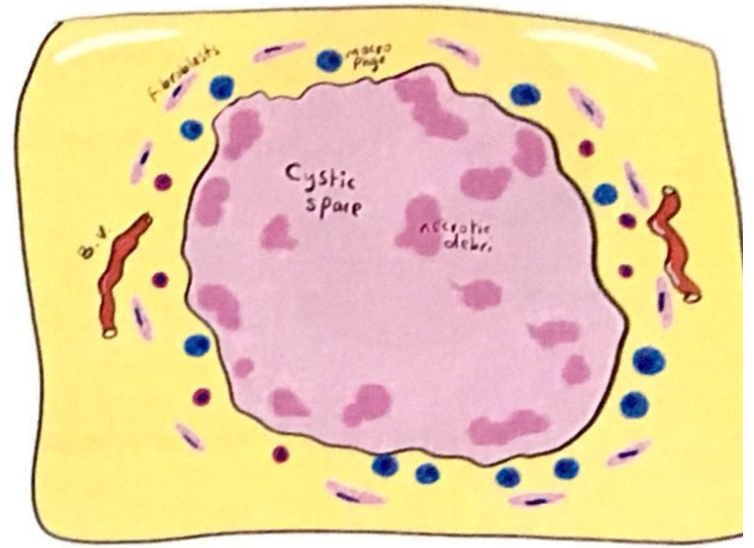


Liquifactive necrosis:

- **Cause:** 1- Proteolytic enzymes in **Abscess**
2- **Brain** infarction
3- Liquifactive enzymes of **amoeb**
- **Gross:** dead area is "liquified", and "yellowish"



- **Microscopic:** tissue became **structureless homogenous** (complete liquefaction) → **cystic** change or cavitation
Surrounded by **inflammatory cells** & **macrophage**
Surrounded by **fibroblasts** or **glial cells** (in CNS) & new capillaries



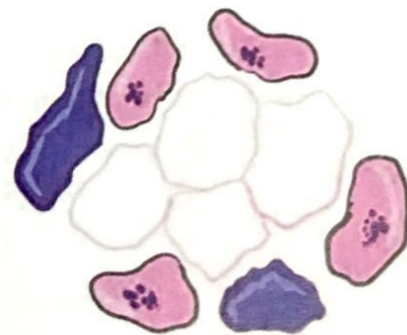
Fat necrosis:

- It is necrosis of "Fat cells" in adipose tissue
- **Cause: 1- Traumatic**
- Trauma of **subcutaneous fat**, may lead to ruptured fat cells, and deposition of calcium salts in the area of fat necrosis, giving hard palpable mass.

2-Enzymatic

Acute pancreatitis → release of **lipase** → fat cell necrosis in **omentum** → release of fatty acids (FA) → FA + intracellular Ca → Calcium soaps (**Saponification**)

- **Gross:** dead area is "firm chalky", and "white "
- **Microscopic:** - Injured fat cells (shadows)
- Calcification (basophilic)
- inflammatory cells and giant cells

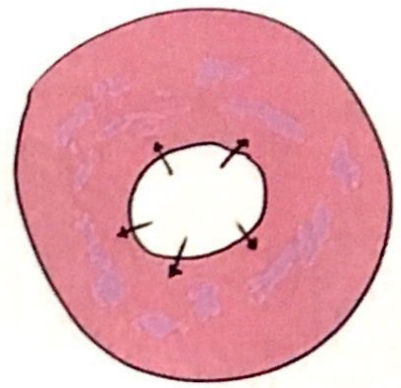


in case of hard mass in the **breast** of young female, traumatic fat necrosis should be taken in consideration before diagnosis of **cancer breast**.

⑤ **Fibrinoid necrosis:** Deposition of fibrin-like material

- Autoimmune vasculitis (e.g. polyarteritis nodosa)
- Arterioles in malignant hypertension
- Aschoff nodule (in rheumatic fever)

Microscopic: homogenous **eosinophilic** deposit in the wall



N.B. **Autolysis:** means damage of cell by its own lysosomal enzymes mainly postmortem

Fate of necrosis

- **Inflammation:** All types of necrosis initiates inflammatory reaction
- **Regeneration**
- **Fibrosis:** depends on type of tissue and severity of injury
- **Capsulation:** fibrosis around the periphery of necrotic area
- **Calcification:** deposition of calcium salts inside dead tissue
- **Putrefaction (Gangrene) :** if infected with certain types of bacteria

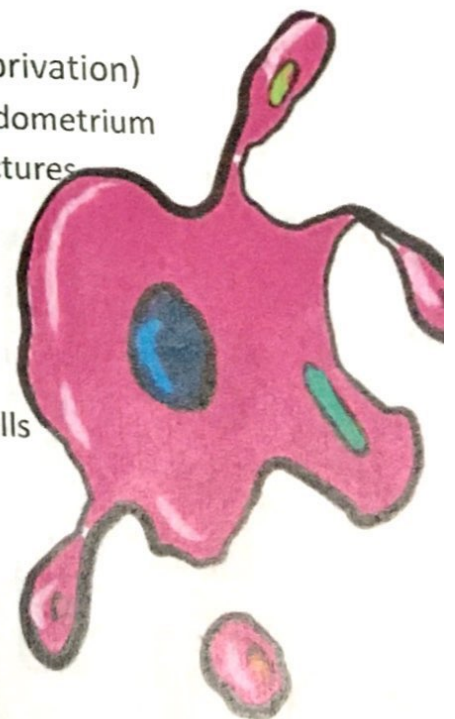
Apoptosis

Definition: Coordinate death of single cell or group of cells, by energy-dependant **programmed** pathway. *Not accompanied by inflammation*

Causes:

- **Physiological** (mainly **Hormonal** or **growth factor** deprivation)
 - o Menstruation , hormonal-induced apoptosis of endometrium
 - o Embryogenesis, absence of some embryonic structures
 - o Thymus atrophy
- **Pathological** (disease-induced) **3 H + 3 C**
 - o HCV → Liver cell apoptosis (**councilman body**)
 - o HLA mismatch → graft rejection by Cytotoxic T cells
 - o Hypoxia and radiation
 - o Chemotherapy → tumor cell apoptosis
 - o Cancer prostate (after orchiectomy)
 - o Cerebral apoptosis (in Alzheimer)

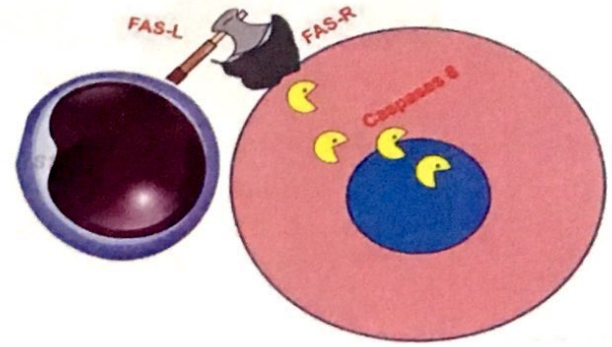
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Mechanism:

Extrinsic:

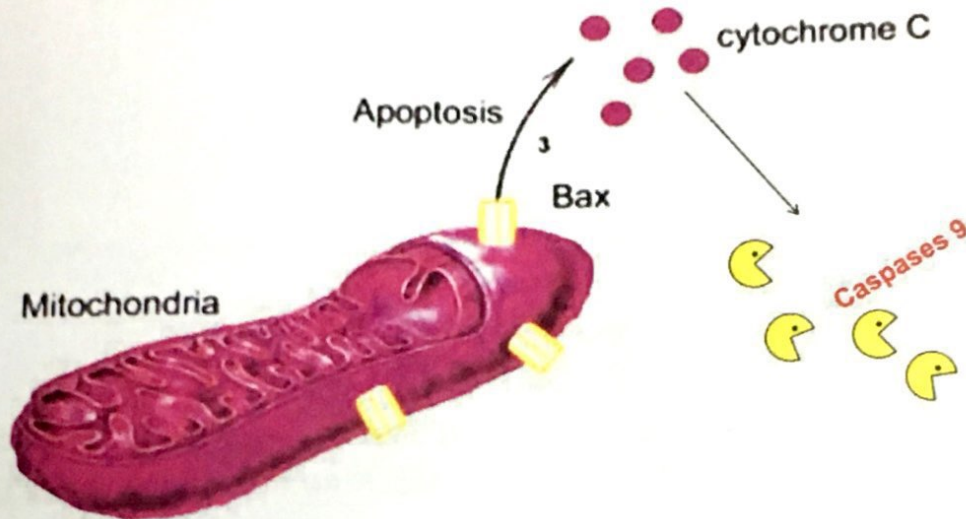
Expression of **FAS** receptors on cell → bind with **FAS-L** on lymphocytes → activation of caspases (**caspase 8**) → apoptosis



CD8
killer cells (Type T)

Intrinsic (mitochondrial): mediated by regulation of Bcl2

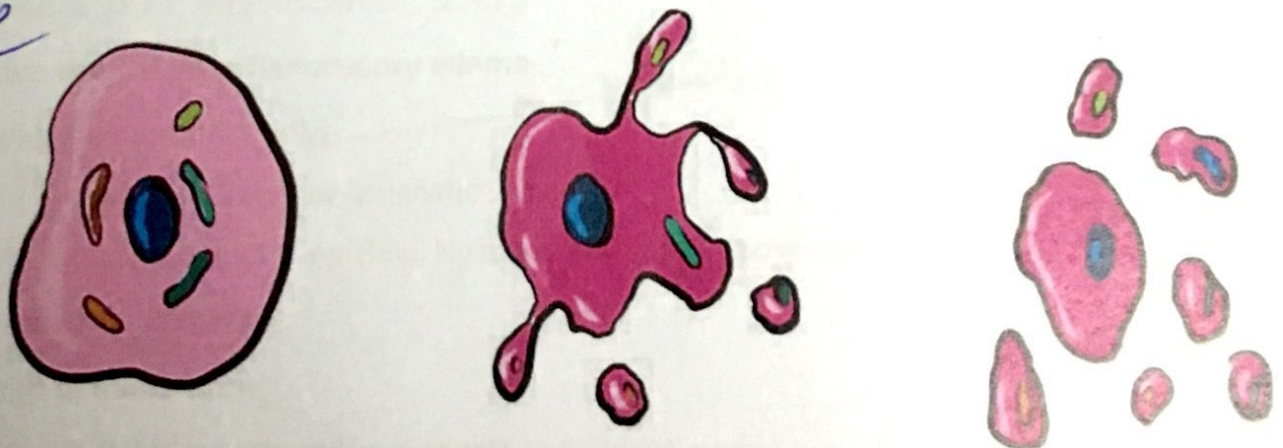
family genes → activation of Bax & bak, inhibition of Bcl → **Bax** is forming mitochondrial channels → increased mitochondrial permeability → release of **cytochrome C** → activation of **caspases 9** → apoptosis



Morphological changes :

- Cell shrink in size & convoluted
- **Condensation** of chromatin or fragmented
- Condensed **organelles**
- Cell divides into smaller **apoptotic bodies**
- Apoptotic bodies are **phagocytosed**

Fate



5/20/8

Abdelrahman Khalifa
26/6/0

	Necrosis	Apoptosis
Definition	Cell death with damaged cellular content	Programmed cell death
causes	Pathological injury <i>group of cells</i>	Physiological or pathological <i>Single cell or group of cells</i>
mechanism	Controlled by ATP depletion	Controlled by genes, enzymes and hormones <i>estrogen and progesterone</i>
microscopic	-large cell -damaged membrane -damaged organelles & lysosome -damaged nucleues	-Small cell -intact membrane with blebs -condensed organelles -condensed chromatin
Molecular changes	Libration of lysosomal enzymes Free radicals Lack of ATP	Gene regulation Bcl2, Bax, P53 and FAS
inflammation	present	absent
fate	(enumerate)	phagocytosis

Gangrene

Massive tissue **necrosis**, followed by **putrefaction**: Breakdown of dead tissue by saprophytic bacteria → release of H₂S (offensive gas) → formation of Iron Sulphide (black color)

Dry gangrene

Gangrene Caused by arterial occlusion (e.g. Thrombus) → followed by tissue dryness (mummification) → then putrefaction e.g. **Senile dry gangrene of the foot**

Pathogenesis:

- Ischemia (P.F. : Atherosclerosis, & H.F.)
- Tissue necrosis & inflammatory edema
- Dryness (mummification)
 - Edema is drained by lymphatics, and veins.
 - Evaporation of tissue fluid. No more fluid supply (ischemia)
- Putrefaction & spread
- Line of demarcation
 - Putrefaction stop at the area with **good blood** supply
 - The **red line** separating healthy tissue from putrefied tissue
- Granulation tissue
 - Healing starts from line of demarcation → extend distally

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blood vessel
آخر امتداد عروق الدم

- Line of separation

- The line separating GT from remaining unhealed putrefied tissue

- Self separation (amputation)

- The remaining dead tissue begin to separate spontaneously leaving conical stump

examination
tissue
New fiber
New capillary
Skin
ملاحظة
تأخر
Stamp



Ischemia



Necrosis



Mumification



Putrefaction



Demarcation



Separation

Sheep

	Dry gangrene	Moist gangrene
Aetiology	Arterial occlusion Atherosclerosis – Burger -Reynaud	Arterial occlusion in moist areas Moist tissue (mouth, cervix) Intestine (strabgulation) → occlusion of vein D.M. (excess inflammation & fluid) → non evaporation Bed sores (arterial & venous compression)
Ischemia	present	present
Edema	present	more
Mummification	present	No mummification
Putrefaction and spread	Slow	Rapid
Line of demarcation	present spread توسع تأخر	No line of demarcation
Line of separation	Present	No line of separation
Self separation	present	No self separation
Complications	Mild Toxemia (sapremia)	Rapid spread Severe Toxemia (sapremia)

Gas gangrene

Putrefaction of muscles, through infection of deep wounds

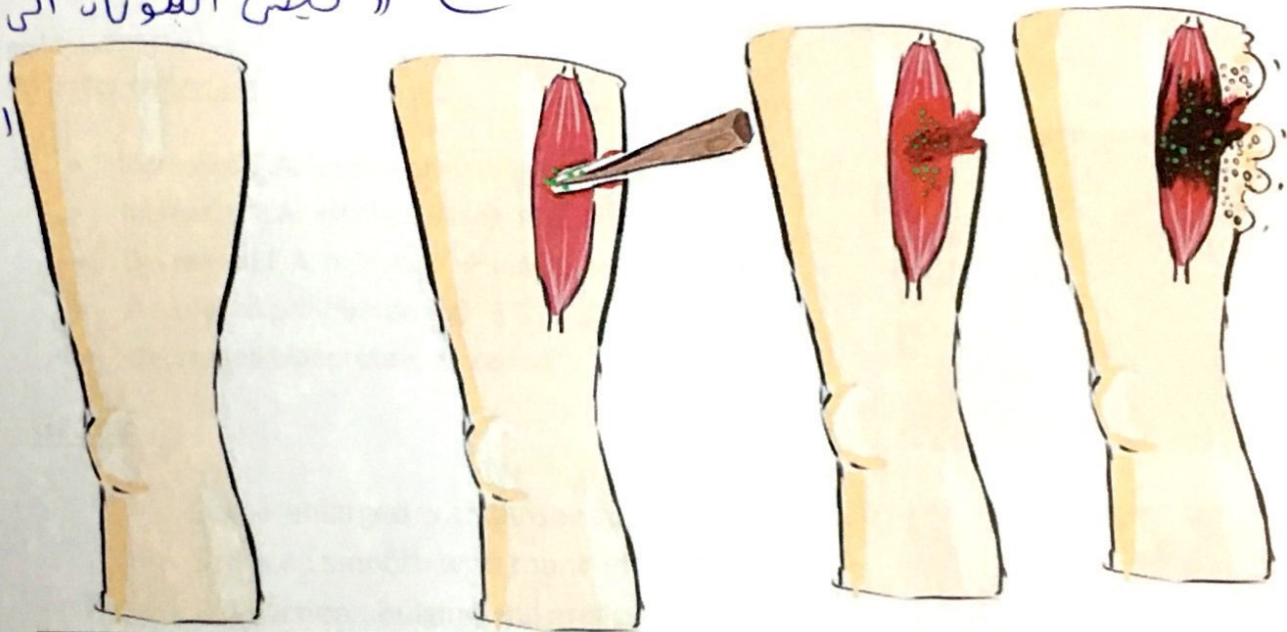
Aetiology:

1. Infected deep wounds by anaerobic Clostridia from soil
2. Infected wound during colon surgery

Pathogenesis:

3. Muscle **necrosis** + Hemolysis → **Red dead muscle**
4. Putrefaction → extensive gas (H_2S) accumulation + **Black swollen muscle**
5. Excessive gas → Crepitation

Fate: Severe toxemia



Fatty changes

Definition: Reversible cell injury, showing neutral fat (triglycerides) accumulation in parenchyma

Causes: causes of cell injury, Mostly: hypoxia, bacterial toxins, chemicals

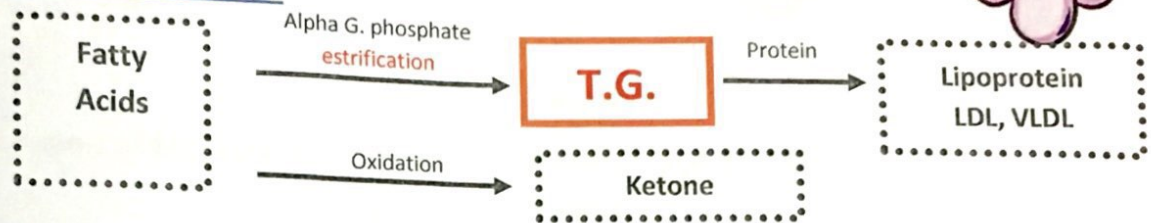
Sites: Liver (most common) – Heart – Kidney

causes of fatty liver

- Hyperlipidemia (Congenital – Obesity – DM – Alcohol the most common)
- Drugs & toxins (CCL₄, Steroides)
- Diseases (H.P. – Anemia – TB)

Pathogenesis of fatty liver

Normally:



In Fatty changes:

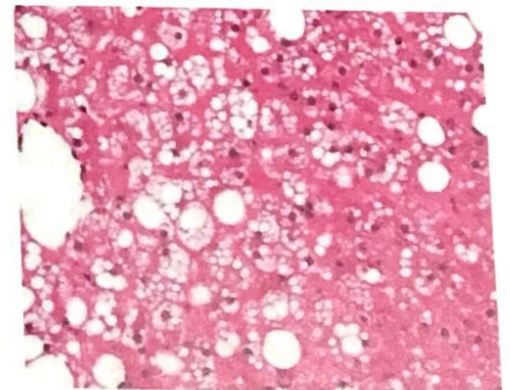
- Increased F.A. intake, or **synthesis** → T.G.
- Increased F.A. **estrification** → T.G.
- Decreased F.A. **oxidation** → increased F.A. → T.G.
- Decreased **protein carriers** → T.G. accumulation
- Decreased **Lipoprotein excretion**

Gross:

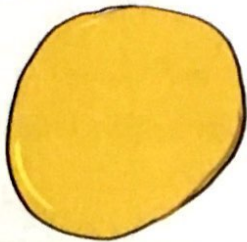
- Size : enlarged with tense capsule
- Surface : smooth with rounded borders
- Cut section : bulging and greasy
- Color : Yellow
- Consistency : Soft Greasy

Microscopic:

- Cells: swollen, intact membrane, with clear cytoplasmic vacuoles (microvesicular steatosis) → large single vacuole (macrovesicular) → signet ring cells
- Ruptured fat cells → Fat cyst & lipogranuloma
- Staining: Sudan III, IV, black, Osmic acid, Oil red



Fatty changes of the Heart

Diffuse fatty change	Patchy (focal) fatty change
Severe	Mild
In cases of Toxemia , severe hypoxia	In case of Anemia
Yellow in color	Yellow & brown (Tabby cat/ tiger skin)
	

Fatty infiltration

Accumulation of fat inside connective tissue due to obesity or chronic diseases.
(e.g. Heart , pancreas)

Cholesterol deposition:

- **Macrophages** (in old hemorrhage or necrosis) → foam cells
- **Atherosclerosis** (in macrophages 'foam cells' inside arterial wall)
- **Xanthoma** (in macrophage of Skin in cases of hyperlipidemia)



Cholesterosis: accumulation of cholesterol in G.B. epithelium

Melanin pigment

Tyrosine → converted into brown melanin (by tyrosinase enzyme) → engulfed by macrophage (melanophores)

Hyper pigmentation

○ Generalized

- **Chloasma:** butterfly color in face and breast (estrogen-progestron)
- **Adisson's:** due to increased ACTH, MSH

○ Localized Patchy

- **Sun Freckle**
- **Melanocyte tumors** (nevus- melanoma)



Hypo pigmentation

○ Generalized

Albinism : congenital 'autosomal-recessive' tyrosinase deficiency

○ Localized Patchy

- **Leukoderma** which is congenital or secondary to Syphilis or Leprosy
- **Vetiligo** which is an autoimmune dis.

break of melanocytes → melanin

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Glycogen

In D.M.: due to abnormal glucose metabolism

Glycogen storage disease: genetic, metabolic disease. Accumulation of glycogen in **Liver**, **muscle**, and **heart**. Cells show clear cytoplasm, stained with **Best's carmine**



BAS

rose red

Hemosiderosis

⇒ Hemosiderin

Ferretin accumulates inside tissue **macrophage** (yellowish brown) → stains blue with **Perl** or **Prussian blue**

No tissue damage

Localized Hemosiderosis

- Skin hemorrhage (bruise) → Hemosiderin
- green **billiverdin** → brown **hemosedrin**

Left side heart failure

- Lung congestion → macrophage engulf hemosedrin → H.F. cells (brown induration of lung)

Generalized hemosiderosis

- Hemolysis
- Repeated transfusion
- Increased Iron intake

Engulfed by macrophage of **Liver**, **spleen**, **B.M.**, & **L.N.**

Hemochromatosis

Accumulation of iron in **parenchymatous** tissue → leading to **tissue damage**

1ry Hemochromatosis (bronzed D.M.)

Increased iron absorption (autosomal dominant) → deposition in

- Pancreas → DM
- Liver → pigmented cirrhosis
- Skin → **bronzed color**

2ry hemochromatosis

Prolonged generalized hemosidrosis

Exogenous Pigments

- **Tattoo** (Indian ink → engulfed by macrophage)
- **Anthracois** (Black **Carbon** deposition e.g. smoking, pollution → engulfed by lung **macrophages** → black color in lung and hilar L.N.)



Lipofuscin pigment (Lipochrome)

Definition: Yellowish brown Intracellular, Lipid-derived pigment, due to cell aging (wear and tear)

Pathogenesis: lipid peroxidation + waste products → accumulated in lysosomes

Brown atrophy of the heart :

- **Cause:** Senility (aging) - Starvation - Chronic ischemia
- **Gross:** Reduced size, tortuous coronaries, absent pericardial fat, thin brown muscle
- **Microscopic:** cell size: reduced , cytoplasm: **yellow brown pigment** around nucleus,



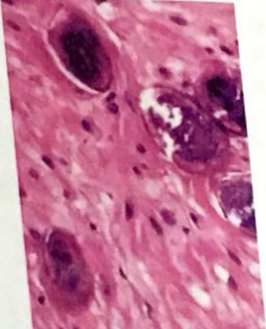
Pathological Calcification

Pathological deposition of **calcium salts** in tissues other than bone and teeth.

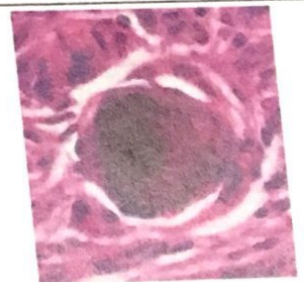
Gross:

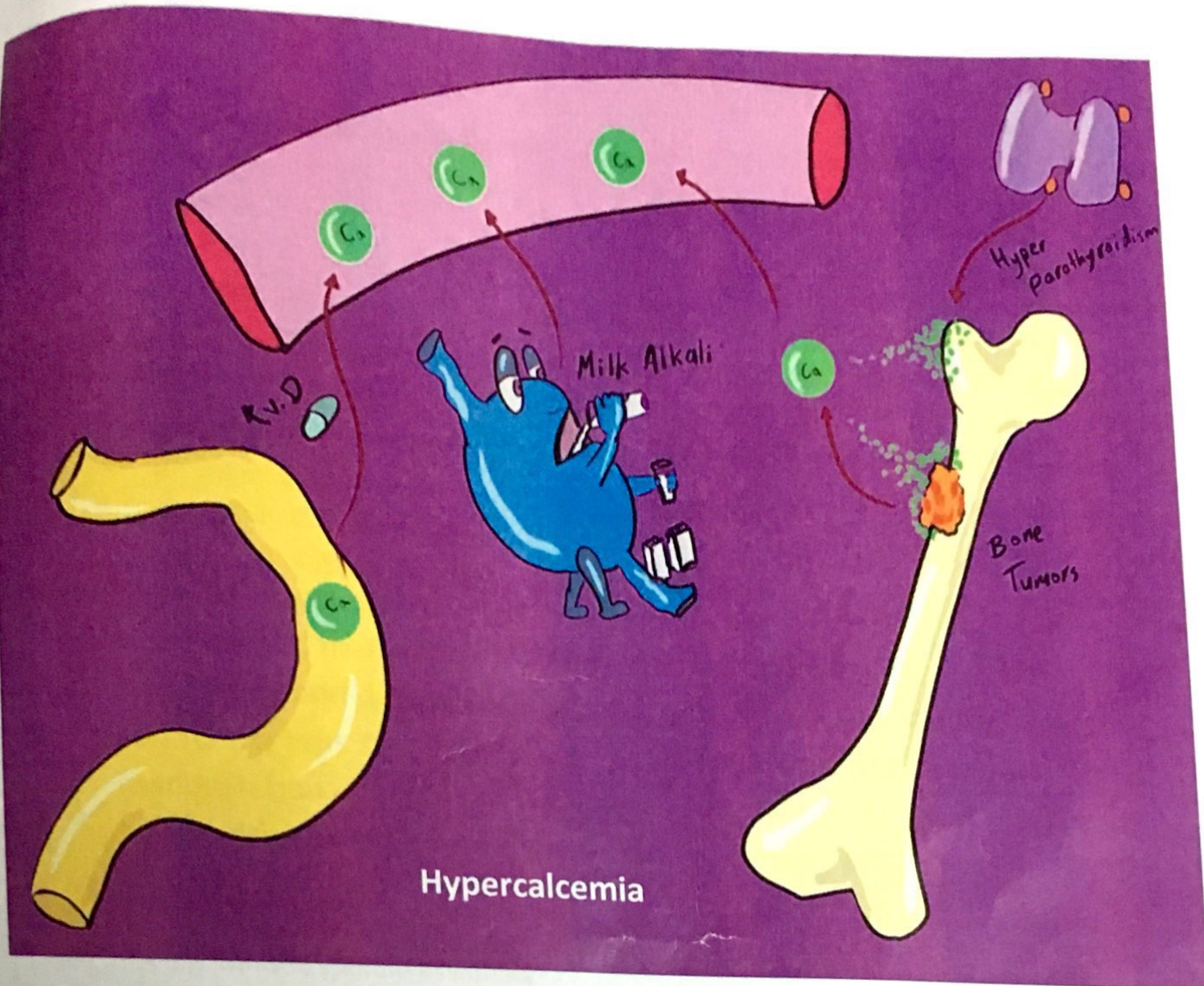
- **Color :** white
- **Consistency:** Hard granular, or chalky

Micro: Basophilic in color, intracellular or extracellular

	Dystrophic calcification	Metastatic calcification
Tissue	Dead tissue, Degenerated tissue	Normal tissue
Serum Ca	Normal (9-11)	Elevated > 11
Causes and sites	Dead: - Necrosis (.....) - Necrotic cancer (tumor) - Dead fetus - Dead parasites and ova - Blood thrombus - Blood hematoma Degenerated: PASS Dead tissue - Psammoma bodies - Atherosclerosis & Monckeberg - Scar $\Rightarrow$ healing of wounds - Stroma of tumors   <i>Handwritten notes:</i> Degeneration, liver, irreversible, tissue calcification	Elevation of serum calcium: 1-Increased absorption: $\uparrow$ Vitamin D (e.g. sarcoidosis) $\rightarrow$ macrophage activate v. D precursor $\uparrow$ Ca (milk alkali syndrome) 2-Increased bone resorption: $\uparrow$ Parathyroid 1ry - 2ry to R.F. - parathyroid like proteins - Bone tumors (multiple myeloma) - Immobilization Serum Ca $\rightarrow$ deposits in alkaline tissues - Renal tubular membrane - Gastric mucosa - Alveolar wall - Blood vessels - rarely synovium <i>Handwritten notes:</i> tissue calcification
Mechanism	- Increased intracellular <u>Ca</u> - Increased intracellular <u>phosphate</u> <u>Calcium phosphate</u> stones	Increased serum calcium and phosphate

Psammoma bodies : Rounded laminated bodies , seen in some tumors
(Meningioma – Papillary carcinomas)





Cell aging

Factors affecting aging

- Internal (Telomere length)
- Environmental (Inhaled pollution)
- Diet (obesity, alcohol)
- Diseases (Atherosclerosis, hypertension, DM)

Mechanism

- After fixed number of cell divisions → **telomerase inhibition** → Shortening of telomere in gene
- decreased senescence (arrest of cell cycle)
- Accumulation of free radicals



- 1) The consequences of Ca influx into the cell include all the following Except:
 - a) Disruption of membrane
 - b) Nuclear chromatin damage
 - c) Increased ATP
 - d) Induction of apoptosis
- 2) You are asked to participate in a research project on myocardial infarction in a rat model. Which of the following occurs in ischemic cell injury?
 - a) Efflux of K^+ and Na^+
 - b) Influx of K^+ and Ca^{++}
 - c) Influx of K^+ and H_2O
 - d) Influx of Na^+ and Ca^{++}
 - e) Influx of Na^+ and K^+
- 3) A 30-year old man with AIDS dementia complex develops acute pneumonia and dies of respiratory insufficiency. At autopsy, many central nervous system neurons display hydropic degeneration. This manifestation of sublethal neuronal injury was most likely mediated by impairment of which of the following cellular processes?
 - a) DNA synthesis
 - b) Lipid peroxidation
 - c) Mitotic spindle assembly
 - d) Plasma membrane sodium transport
 - e) Ribosome biosynthesis
- 4) A well-demarcated lesion with increased cytoplasmic eosinophilia, karyolysis, and intact tissue architecture is characteristic of:
 - a) Tuberculosis
 - b) Acute pancreatitis
 - c) Myocardial infarction
 - d) Brain infarction
 - e) Vasculitis
- 5) An old atherosclerotic man had a minor trauma of the toes which was followed by blackish discoloration of the big toe. Which of the following is responsible for this color:
 - a) Melanin
 - b) Hemoglobin
 - c) Iron sulphide
 - d) Hemosiderin
 - e) Lipofuscin
- 6) Enzymatic digestion is the predominant event in which of the following lesions:

- a) Splenic infarction
- b) Amoebic liver abscess
- c) Tuberculosis
- d) Traumatic fat necrosis
- e) Viral hepatitis

7) A pathologist noted the following findings after light microscopic examination of a section of liver from a chronic alcoholic. Which of the following is an example of a reversible injury?

- a) Pyknosis
- b) Cytoplasmic vacuoles
- c) Rupture of cell membrane
- d) Karyolysis
- e) Karyorrhexis

8) Russel bodies represent intracellular accumulation of:

- a) Proteins in lymphocytes
- b) Proteins in macrophages
- c) Protein in plasma cell
- d) Glycogen in plasma cell
- e) Glycogen in macrophages

9) Stromal fatty infiltration is the stromal deposition of:

- a) Cholesterol crystals
- b) Phospholipids
- c) Free fatty acids
- d) Lipoprotein
- e) Adipose cells

10) Metastatic calcification is most likely to occur in which of the following conditions?

- a) Tuberculosis of the lung
- b) Acute hemorrhagic pancreatitis
- c) Aortic stenosis in a 70-year-old man
- d) Multiple myeloma
- e) Haematoma

Easy Pathology

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Repair

Ainshams 2018 - 2019

Repair

Replacement of damaged tissue by healthy new tissue.

<u>Regeneration</u>	<u>Connective tissue (Fibrosis)</u>
Replacement of dead tissue by tissue of the same type	Replacement of dead tissue by Fibrosis , or Gloiosis (in CNS)
Regeneration of epithelial cells	-In case of frame work damage -In case of organization (following <u>fibrinous inflammation</u>)

Depends on : Rate of proliferation & death + Type of cell

Classification of cells

	Labile	Stable	Permanent
Definition	Continuous dividing cells , with <u>High ability</u> to regenerate	<u>Limited ability</u> of regeneration in response to injury within limits. Healing occurs by <u>regeneration</u> and <u>fibrosis</u>	Not able to regenerate or divide. Heal by fibrosis or gliosis
Response to injury	Mild-severe injury → <u>regenerate</u> successfully	Mild injury → <u>regenerate</u> Severe (damaged framework) → <u>regeneration</u> + <u>fibrosis</u>	Injury → <u>fibrosis</u> or <u>gliosis</u>
examples	Surface epithelium and cornea Duct epithelium Hematopoietic & Lymphoid 	Mesenchymal (fibroblasts-Cartilage - bone - smooth muscles - endothelium) Parenchymatous organs (liver - kidney (PCT) - endocrine glands)  <i>Smooth muscle is stable</i>	Heart & skeletal muscle → fibrosis Nerves → gliosis Lens → fibrosis Glomerular podocytes → fibrosis 

Organization : fibrosis in tissue spaces occupied by inflammatory exudate (e.g. Sero-fibrinous inflammation of pleura)

→ *Air fibrosis inside with fibrin*

also to F Fibrin → macrophage → induce fibrosis

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Stem Cells

Immature unspecialized cells, able to divide, and differentiate into specialized cells with preservation of its population

Sources and Types:

- **Embryonic** : from inner mass of blastocyst **high potency** (totipotent, pluri)
- **Adult stem cells**: (e.g. Bone marrow, Tissue stem cells) **limited potency** (multi potent, oligo , uni)

How to identify stem cells in tissue? by certain markers , e.g. CD34 , CD38



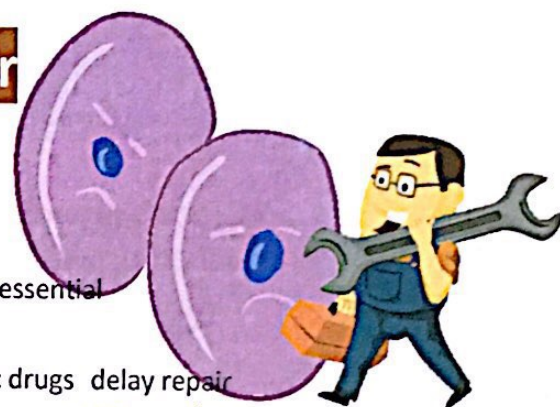
Differentiation potency: ability of differentiation

- **Toti potent**: gives all type of cells and giving complete organ (e.g. germ cells)
- **Pleuri potent**: gives all type of cells except placenta , cannot give fetus, only giving embryonic tissue (e.g. inner mass of blastocyst)
- **Multi potent**: multiple type of limited related cells (e.g. *hematopoietic cells* → *blood cells*)
- **Oligopotent**: gives few types of cells (e.g. *Lymphoid* & *myeloid*)
- **Uni potent**: gives single cell type (e.g. *hepatocyte*)

Factors affecting repair

1. General & Local factors:

- **Age**: Healing is better in young age
- **Nutrition**: Proteins – vitamins (C – D) – Zink are essential
- **Diseases**: DM – Cushing
- **Drugs**: Cortisone (reduce fibrosis) – cytotoxic drugs delay repair



Angiopathy

Ischemia - Infections & foreign body - Injury severity & site

Tissue type

Defective leukocyte function

2. Growth factors:

hormone-like, acts locally (autocrine & paracrine) to help division of cell (G1 phase)

Mechanism: Bind to cell receptors →

- 1-affect expression of **genes** whose products promote mitosis
- 2-stimulate **synthesis** of cellular proteins involved in **mitosis** :

cell Proliferation – differentiation – migration – synthesis of proteins – prevent apoptosis

Cortisol

TGFB

* إزاي بيقل الليفات Fibrosis

Handwritten notes: *end dermis* (pointing to EGF), *platelets driven* (pointing to PDGF), *USMLE* (underlined), *Angiogenesis* (circled), *MMPs* (circled), *inhibit epidermal division* (underlined).

G.F.	Source	Target
EGF <i>epidermal</i>	Macrophage, Skin, <i>platelets</i>	Fibroblast, Skin, <i>Keratinocyte</i>
FGF <i>Fibroblast</i>	Macrophage, Fibroblast	Fibroblast, Skin
VEGF <i>Vascular, endothelial</i>	Mesenchymal cells	<i>endothelium</i> , permeability
PDGF <i>platelets driven</i>	Endothelium, Smooth muscle, Platelet	Fibroblast, <i>endothelium</i> , Smooth muscle + AIM
USMLE		<i>Angiogenesis</i> (circled) <i>Inflammatory response</i> (chemotaxis & Integrin expression) <i>MMPs</i> (circled), fibronectin, Hyaluronic AIM <i>MMPs inhibition by TIMP</i> <i>inhibit epidermal division</i>
TGF beta (stimulatory & inhibitory)	Macrophage, Fibroblast	

3. Extracellular matrix:

- Found in:
 - Interstitial matrix between cells & C.T. (Fibronectin, collagen, elastin)
 - Basement membrane secreted by epithelium & mesenchyme (collagen IV, laminin)
- Components:
 - Structural proteins (collagen) *صلب*
 - Hydrated gel for flexibility (proteoglycans – Hyaluronic acid) *طري*
 - Adhesives between matrix components and cell (Glycoproteins) *لاصق*
- Role:
 - Support & Strength
 - Cell growth and differentiation (integrin family)
 - Slit Filtration in Some areas (kidney)
 - Storage of certain substances (e.g. GFs)

Healing by Regeneration

B.M.: blood loss → Colony stimulation factor CSF → activation of B.M. → blood cells

Hepatectomy: removal of 40-60% of Donor liver → stimulate replication of hepatocytes

In severe injury and inflammation → **disturbed framework** → regeneration + fibrosis (scar)

liver cirrosis → *Regeneration surrounded by Fibrosis*

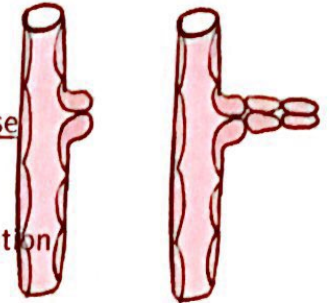
أنحون الحال - تخذ الحال - أمحل حال - حال التظييل

Healing by fibrosis

In stable cells (severe injury) – In permanent cells – In labile epithelium (damaged stroma)

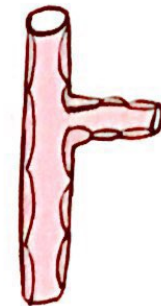
1. Angiogenesis

- **Vasodilatation** (mediated by N.O.) and permeability(VEGF)
- Damage of basement membrane of existing blood vessels by collagenase
- **Endothelial** cell migration outside capillaries
- **Canalization** of endothelial bud and anastomosis → capillary tube formation (leaky vessels due to loss of endothelial junctions & VEGF) → edema
- Migration of **pericytes** (from small vessels) & smooth muscle (from large vessels)



Some vessels are formed by **Endothelial precursor cells**, coming from bone marrow

Growth factors involved in Angiogenesis: **FGF** – **NO** – **VEGF**



2. Fibroblast migration & Granulation Tissue formation

- **Fibroblast migration** to site of injury (stimulated by **PDGF** - **FGF2** - **TGF-B**)
- Fibroblast **secrete** ECM, collagen I, and collagen III (by the 4th day)
- The tissue now contain: inflammatory cells, new capillaries, collagen I, III, ECM
- This is called **Granulation tissue**, which is **grossly red, moist, and granular**, insensitive and resist infection.

active Fibro
Extra
Cell-nd
matrix

3. Scar formation

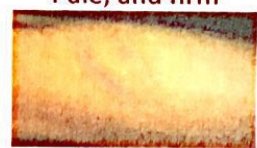
- Increased activity of fibroblasts → Collagen I predominate with excess ECM
- Capillaries became narrow and **obliterated**
- This is called **Scar**, which is **grossly pale**, and firm



4. Scar remodeling:

- Macrophage, fibroblasts & other cells → **MMPs**(collagenase) → reduce collagen
- Contraction of myofibroblasts in some cases (2ry wound) → contracures

N.B. MMPs degrade collagen and are inhibited by TGF-B. TGF-B is inhibited by cortisone

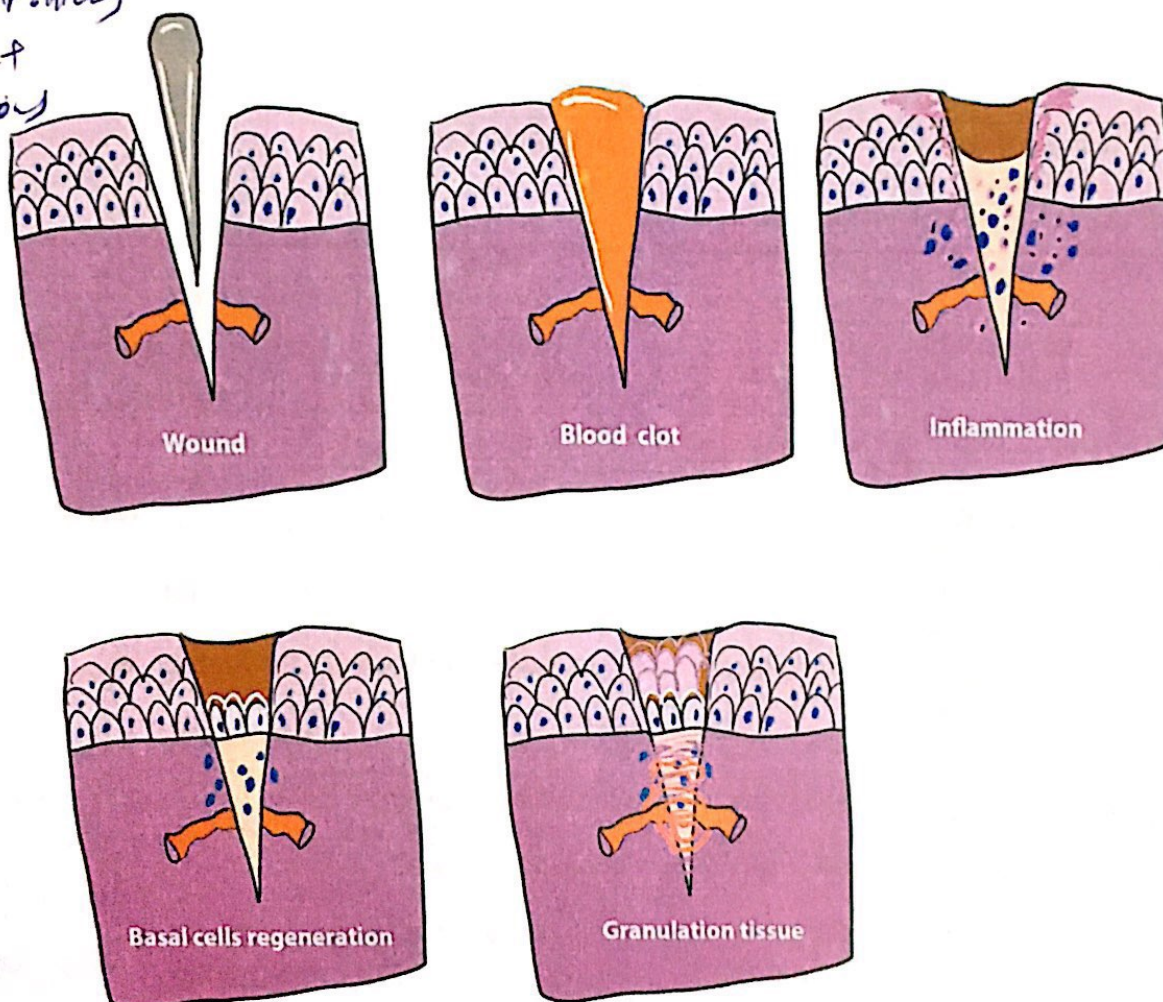
Grnulation tissue	Scar
red, moist, and granular, insensitive, bleed on touch 	Pale, and firm 
<u>inflammatory cells</u> , <u>new capillaries</u> , <u>collagen I, III</u> , <u>ECM</u> , activated fibroblasts	Obliterated capillaries, Collagen I, ECM, elastic tissue, Inactive fibroblasts

Healing of Wounds

Pathogenesis:

- **Blood Clot formation** : protects from infection - RBCs → hemostatin → chemotaxis
- **Inflammation (1st day)** : neutrophils at the margins, followed by macrophages (3rd day) → phagocytosis & GF secretion
- **B.M. & basal layer regeneration (2nd day)** , with complete epidermal regeneration and keratinization by the 5th day.
- **Granulation tissue formation** in dermis (3rd day) : describe? (neovascularization and collagen begin at the margins)
- **Surface keratinization & G.T. is filling the gap 'bridging' (5th day)**
- Excess collagen → capillary obliteration (14th day)
- **Scar maturation** by the 1st month, but tensile strength takes 3 months to be 80% (10% immediately after suture removal, while 70% with sutures)
- Skin appendages do not regenerate

Hand. W. 1/2
s-cut
skin 1/2

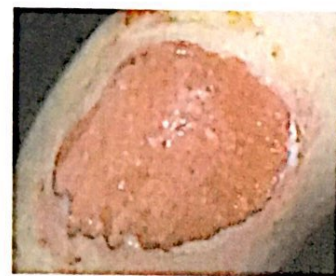


Types:

	1ry union	2ry union
wound	Clean (no infection) Closed or approximate edges 	Infected, or F.B. Gap wound 
mechanism	(describe)	(Same) but Granulation tissue takes place before basal layer regeneration From base → upwards the from margins → inwards
Inflammation	Less	more
G.T.	Less	more
Scar contraction	Linear not contracted	Contracted irregular (by myofibroblasts) contracts within 6 weeks to 5-10% of its original size
duration	short	longer
complications	Not common inclusion cysts	More common enumerate?

Complications of wound healing:

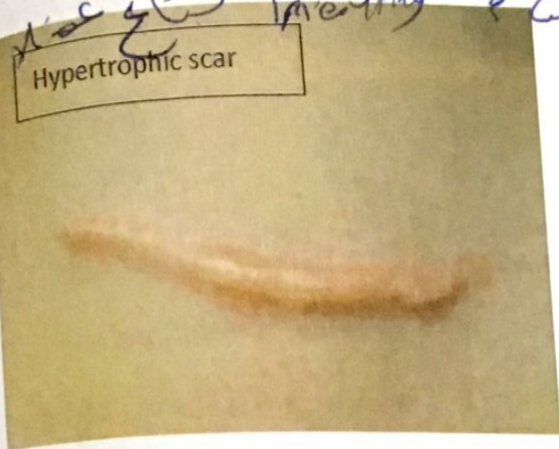
- Infection → pus
- Excess G.T. (proud flesh) → failure of epidermal growth
- Excess scar



- Hypertrophic scar**: elevated scar not exceeding wound edges
- Keloid**: excess scar beyond wound edges (Familial dark races – F.B.)
- Contraction of scar** → Contractures (cicatrisation) With deformity and limitation of movement
- Cyst** (implantation epidermal cyst): the wound is lined by skin and filled with keratin.

- General Pathology
- **Carcinoma** (Squamous cell carcinoma) : in chronic scar of Marjolin's ulcer
 - **Minimal scar** formation → wound splitting , incision hernia, ulcer, sinus, fistula
 - **Hemosiderosis** (localized hemorrhage)

Hypertrophic scar



Keloid



Contractures



Cell cycle

USMLE

G1: mRNA & proteins synthesis**S:** DNA replication**G2:** DNA correction**M:** division : prophase – metaphase- anaphase-telophase**G0:** resting phase

Intracellular proteins that promote mitosis: Cyclin & CDK which are degraded after mitoses

Quiz

1- The following injuries Show healing by regeneration EXCEPT: (d)

- a) Healed Bone fracture
- b) Healed Skin wound
- c) Liver cirrhosis infarction
- d) Healed myocardial

2- Healing by fibrosis occurs in all of the following situations EXCEPT: (b)

- a) Healed Renal infarction
- b) Healed Skin wound
- c) Old cerebral infarction
- d) Healed myocardial infarction

3- Which of the following growth factors has an inhibitory effect: (b)

- a) b-FGF
- b) TGF Beta
- c) PDGF
- d) none

4- Granulation tissue could be formed in the following situations EXCEPT: (d)

- a) Wound healing infarction
- b) Healing of myocardial
- c) Healing of perforated peptic ulcer
- d) Healing of brain infarction

5- Granulation tissue is formed of the following components EXCEPT: (c)

- a) Inflammatory cells
- b) Fibroblasts & collagen
- c) Epithelioid cells
- d) Capillaries

6- A surgical wound is infected and contains pus. Healing occurs by: (b)

- a) 1ry union
- b) 2ry union

c) Fibrosis only

d) Regeneration only

7- Which of the following situations is true in healing of CNS: (c)

a) Regeneration of damaged nerve cell

b) Fibrosis

c) Gliosis

d) none of the above

8- Sero-fibrinous inflammation heals by by: (a)

a) Organization

b) Regeneration

c) Fibrosis only

d) none of the above

9- A Keloid is devoid of: (c)

a) Epidermis

b) Collagen

c) Skin adnexa

d) Fibroblasts

10- Contraction of wound scar is caused by: (c)

a) MMPs

b) Fibroblasts

c) Myofibroblasts

d) none of the above

11- Cells which never regenerate are called: (c)

a) Labile

b) Stable

c) Permanent

d) none of the above

12- Cells able to enter cell cycle without injury are called: (a)

a) Labile

b) Stable

c) Permanent

d) none of the above

13- Cells which heal by both regeneration and fibrosis are called: (b)

a) Labile

b) Stable

c) Permanent

d) none of the above

14- A pathogen is causing colonic ulcer deep to submucosa, Healing of this ulcer is done by : (c)

- a) Regeneration
- c) Both

- b) Fibrosis
- d) Non

15- Stab wound is penetrating chest wall, with evident pleural injury, Healing of pleura will result in: (d)

- a) Fibrosis formation
- c) Adhesions

- b) Granulation tissue
- d) All of the above

16- Wound contracture is : (a)

- a) induced by myofibroblasts wound
- c) induced by suppression of fibroblasts

- b) more common in 1ry
- d) All of the above

17- Musculosa of GIT heals by: (c)

- a) Regeneration
- c) Both

- b) Fibrosis
- d) Non of the above

18- Proud Flesh is defined as: (b)

- a) Contracted scar
- c) Healing by 1ry intention tissue

- b) Excess granulation tissue
- d) Formation of granulation

20- Hypertrophic scar is: (d)

- a) Contracted scar edges
- c) The same as Keloid

- b) Scar extending beyond wound
- d) Non

21- Proliferation of endothelium is mediated by all of the following EXCEPT: (c)

- a) VEGF
- c) all
- b) PDGF
- d) non

Cases Bone Fracture Healing

Case1

A young boy had a car accident. X-ray showed fracture femur. 10 days later X-ray revealed Callus.

- 1-What is the type of this callus?
- 2.Enumerate possible causes of malunion in this patient?

Case2

A 50 years diabetic Female having appendectomy 2 weeks ago. Now she is feverish. Surgical wound is red and discharging pus. After 2 weeks of management, the wound is partially closed, but with remnant skin opening discharging colonic content.

- 1.What is type of wound healing in this case
- 2.Enumerate steps
- 3.Enumerate complication
- 4.What is the diagnosis of this skin opening
- 5.Enumerate possible causes leading to these complications

Case3

Neuroma

Following crushing limb injury in a young man, a painful nerve mass is found.

- 1.What is the diagnosis
- 2.Explain presence of this mass

Case4

An old male was performing partial nephrectomy due to renal carcinoma.

- 1.What is the type of renal cells according to regenerative ability? *exfoliation*
- 2.If the framework of this kidney is damaged, mention the type of healing
- 3.Enumerate steps of healing in this case

1) A young man has a deep wound in his hand. This wound healed but the site showed raised ulcerated nodular scar. Which of the following terms best describe this complication:

- a) Secondary union
- ☒ b) Keloid formation
- c) Exuberant granulation tissue
- d) Organization

2) Which of the following factors is most likely involved in promoting angiogenesis: (c)

- a) Epidermal growth factor
- b) Platelet derived growth factor
- c) Basic fibroblast growth factor
- d) Transforming growth factor beta
- e) Macrophage migration inhibitory factor

3) The inner cell mass of the blastocyst is the source of (a)

- a) Pluripotent stem cell
- b) Multipotent stem cell
- c) Oligopotent stem cell
- d) Unipotent stem cell
- e) None of the above

4) A male patient 30 years old has a gun shot. The complication that can follow his wound healing include all except: (d)

- a) Dermoid cyst
- b) Keloid
- c) Ulceration
- d) Pigmentation

5) Give reason for :

- a) After major surgery, normal activities can be resumed after 3 months.
- b) Wound contraction occurs in wounds healing by secondary intention.
- c) Regeneration of the liver occurs after surgical removal of 40-60 % of the liver in living donor transplantation.
- d) Wound healing in patients on steroids may be complicated.

6) Compare between:

- a) Primary & secondary union of wounds.
- ☒ b) Keloid & Exuberant granulation tissue.
- ☒ c) Stable cells, labile cells & permanent cells.
- d) Totipotent embryonic stem cells & multipotent embryonic stem cells.

Easy Pathology

Dr. Abdelrahman Khalifa

Hemodynamic disorders

Ainshams 2018 - 2019

Edema

Pathological Accumulation of fluid in interstitial tissue and body spaces
Anasarca: generalized edema affecting S.C. tissue, serous sacs, and viscera
Factors affecting fluid accumulation:
Increased hydrostatic pressure in capillaries – reduced osmotic pressure



Types, mechanisms Causes & pathogenesis:

Hydrostatic (increased hydrostatic pressure in veins and capillaries)

- **Generalized**: Right s. H.F. → generalized venous congestion → inc. H. Pressure
- **Localized**: Venous obstruction (Thrombus DVT), Vein compression (Tumor, pregnancy)

Osmotic

- **Nutritional** (decreased intake – increased loss e.g. Famines & starvation)
- **Enteropathy with protein loss** (Maldigestion or malabsorption)
- **Liver failure** → decreased synthesis of albumin
- **Nephrotic syndrome** → proteinuria (> 3gm/day)

○ **Hypoalbuminaemia** → decreased **plasma osmotic pressure** → escape of fluid into interstitial tissue → **decreased renal perfusion** → **salt and water retention** → more edema

Osmotic

Lymphatic (Lymphatic obstruction → lymph fluid accumulates in tissue)

- **Congenital aplasia** (Milroy disease) *آفت اللمفاوية الخلوية*
- **Lymphangitis** e.g. Filariasis → Edema of L.L and scrotum (elephantiasis) *في اللمف*
- **Malignant tumors** → lymphatic obstruction (e.g. Peau de orange appearance in breast cancer)
- **L.N. removal** (e.g. In radical mastectomy → L.N. removal → edema of the arm after few years)
- **Radiotherapy** → following cancer breast → edema of the arm



Lymphatic → ↑ Fibro

Fibrosis

*non-perf
ede*

Na & water retention → increased hydrostatic P.

- **Nephritic syndrome** → inflammation of the kidney → Renin → increase aldosterone
- **Adrenal cortical tumors** → hyperaldosteronism → salt & water retention
- **Right sided H.F.** → renal hypoxia → Renin → aldosterone

في اللمف
Lymph

Increased capillary permeability (inflammatory mediators, or hypoxia), more common with Allergy due to insect bites.

Types of edema

Generalized edema

- **Cardiac** (start in both L.L. (gravity) → then generalized "anasarca")
 - Right S. H.F. → general venous congestion → increased hydrostatic pressure
 - H.F. → real hypoxia → Renin → aldosterone → salt & water retention
 - H.F. → capillary hypoxia → increased permeability
- **Hepatic** (start as Ascitis → then generalized)
 - **Cirrhosis** → portal hypertension → ascitis
 - **Liver failure** → HypoAlbuminemia → osmotic edema
- **Renal** (start periorbital → then generalized)
 - **Nephritic** (G.N. → Renin → aldosterone)
 - **Nephrotic** (Proteinuria → decreased osmotic pressure)
- **Neutritional** (hypoproteinemia) starts periorbital . Mechanism of Osmotic...



Localized edema

- **Obstructive** (venous obstruction – lymphatic obstruction)
- **Inflammatory**

Pathological features

- **Subcutaneous edema**
 - **Pitting** (soft)
 - **Non pitting** (Hard): lymphatic edema → excess C.T. proliferation → firm
- **Effusion** (fluid in serous sacs, e.g. hydrothorax, pericardial effusion)
- **Pulmonary edema**: due to left sided heart failure , Mitral stenosis , or due to ARDS → Lung congestion → increased hydrostatic pressure in pulmonary capillaries → accumulation of transudate in alveoli.
Lung is heavy – C/S contains frothy (air and fluid) & bloody fluid

Microscopic picture & lab analysis:

Separation of EC matrix

Exudate : protein >4gm , S.G.>1020
S.G.<1012

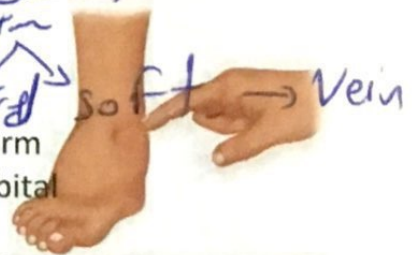
Transudate protein <1gm% ,

Complications of edema

Skin: cellulitis & delayed wound healing

Lung: Infection , decreased ventilation (fluid in air spaces)

Cerebral: Compression of vessels & herniation (death in case of brain stem compression, due to vascular compression)



Acute Respiratory Distress Syndrome

Congestion

Passive Accumulation of blood inside veins, due to obstruction or decreased venous return

Congestion	Hyperemia
<u>Passive</u> <u>venous</u> obstruction Decreased blood flow Veins and capillaries	Active <u>arteriolar</u> dilatation Increased blood flow arterioles
Pathological (generalized – localized)	-Physiological (digestion or in muscle during effort) -Pathological (inflammation)
deoxygenated blood → Tissue hypoxia	Increased Oxygen supply



Causes of Congestion

Localized

- Venous thrombosis (e.g. DVT)
- Compression (e.g. Tumors, portal fibrosis, Pregnancy)
- Ligation or twisting (e.g. surgical ligation, intestinal volvulus)

Generalized

- Acute generalized venous congestion :
Acute H.F. (e.g. Pulmonary embolism)

- Chronic generalized venous congestion: Chronic Rt. sided. heart failure
caused by: Mitral stenosis – Pulmonary stenosis – Lung fibrosis – Emphysema

Pathological manifestations of Chronic generalized venous congestion

1. Cyanosis (due to hypoxia)
2. Dyspnea
3. Congested pulsating neck veins
4. Bilateral lower limb edema → then generalized edema (mechanisms of edema?)
5. Organ Congestion: (e.g. Liver congestion → large tender)

Liver congestion (Nut-meg)

Gross: Large, Nutmeg color (brown hemosiderin + yellow fatty degeneration)

Microscopic:

- C.V. & sinusoids: dilated congested
- Cells: necrosis in central zone, fatty change in midzone
- Kupffer cell contain hemosiderin

Fate: Hemosiderosis → Cardiac cirrhosis



Splenic congestion

Gross: Large, dark red, firm

همگی نشو و ف
Cort (log) capsule

Microscopic:

- Red pulp & sinusoids: dilated congested → ruptured → hemorrhage → forming **gandy-gamma** fibro-sidrotic nodules (hemosedrin + Fibrosis)

- White pulp: Atrophic lymphoid follicles

- Littoral cell contain hemosedrin

macrophages
of spleen

Fate: Hemosiderosis → fibrosis & **Hypersplenism**

بیم
ال
Fibrosis

ک زیادتی فی
بیم الی فی خلاصه ال طبیع

Lung congestion

(N.B. Lung is congested in case of **Mitral stenosis**, or **Left sided heart failure**)

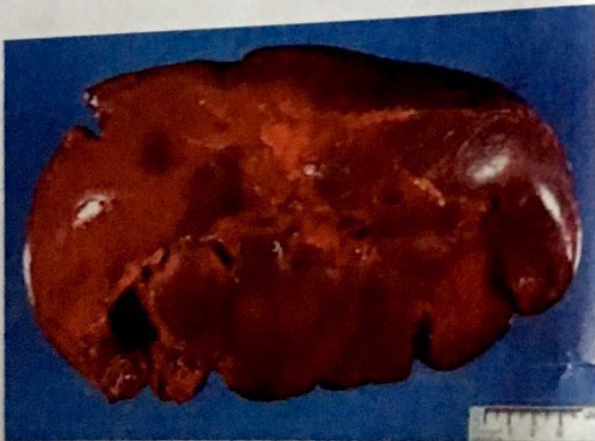
Gross: Large, dark red (bloody & frothy C/S) → brown & firm (**brown induration**)

Microscopic:

- Capillaries: dilated & congested → ruptured capillaries
- Veins: fibrosis of intima – hypertrophy of media
- Alveoli: Thick wall (edema) - lumen contain RBCs & transudate.
- Macrophage in the wall of alveoli → engulf hemosedrin → heart failure cells
- Arterioles: (elastic hyperplasia & hyalinosis) in case of pulm. Hypertension
- Venules: dilated congested

Fate: hemosiderosis → lung Fibrosis (**brown induration**)

Clinical presentation: Hemoptysis



Hemorrhage

Escape of blood outside CVS.

سواد
داخلي
اوعارجي



Causes:

- **Traumatic** : Direct injury of vessels
- **Spontaneous** :

○ General

- Hypertension
- Bleeding tendency (pupura – hemophilia)
- Leukmia
- Vit. C, K deficiency

Bleeding comes from capillaries

○ Local

▪ Vascular damage:

- Arterial: Aneurism – Atherosclerosis – Arteritis
- Venous: Varicose veins
- Capillaries: Congestion, trauma, hemorrhagic diathesis

▪ Vascular penetration: Tumors – TB – perforated ulcer

Types of hemorrhage:

- **External** (eg. Epistaxis, hematemesis, hemoptysis, hematuria, melena "blood from upper G.I.T", bleeding per rectum "blood from lower G.I.T.")
- **Hematoma** deep internal hemorrhage in soft tissue (elevated, not flat)
- **Subcutaneous**

- Petechiae: pinpoint spots in subcutaneous tissue and mucous membranes
- Purpura > 3 mm, more superficial
- Ecchymosis (bruise) > 1cm flat

Subcutaneous hemorrhage begins **Red or Blue** → then **brown** (hsdrin) → then yellow and disappear by macrophage

Effects & complications of hemorrhage: depends on volume, rate, site

- **Small amount:** < 20% → no complications
- **Large amount:** > 20% (1 L.) → Hypovolemic shock
- **Repeated small amounts or Chronic loss:** Iron deficiency anemia
- **Localized hemorrhage** → Hemosiderosis & organ fibrosis

N.B. natural haemostasis is done by: Local vasoconstriction, Clot, then amount is compensated by Tachycardia, bone marrow hyperplasia, & plasma protein restoration.

Shock

Generalized hypoperfusion to vital organs

Cardiogenic	Hypovolemic	Septic	Neurogenic	Anaphylactic
-Myocardial diseases (e.g. M.I., ruptured ventricle, arrhythmia, cardiac tamponade) -Pulmonary embolism - Pump failure → - Reduced COP	-Dehydration: vomiting, diarrhea, burns -Hemorrhage - ↓ plasma volume → - decreased perfusion	-Septicemia (G -ve endotoxin) → high levels of LPS & cytokines 1-Endothelial damage → DIC 2.Leukocyte-mediated → V.D.	-Anesthesia -Nerve injury ↓ spinal cord injury	-Hypersensitivity type 1 Vasodilatation & increased permeability

Post mortem picture of Shock

- Adrenal cortex → depletion
- Vital organs → degeneration & necrosis
- Vasodilatation & increased permeability in organs → Organ hemorrhage edema

↓
 20/8/18

and the other
 damage



Thrombosis

	Thrombus	Clot
Def.	<u>Solid mass</u> of blood elements, formed in <u>circulating blood</u> , inside CVS, during life	Coagulation of fibrin in <u>non-circulating blood</u>
Flow	<u>Circulating</u> blood stasis or turbulence	Non-circulating blood <u>stagnant</u>
Sites	<u>Inside CVS</u> during life	Outside CVS : wound clot Inside CVS: after death – on top of thrombus
Composition	<u>Platelets</u> + fibrin + blood cells Lines of <u>Zahn</u> present	No platelets No lines of Zahn
Attachment	adherent	Loose
Consistency	Firm or friable - Rough	Soft gelatinous - smooth

Causes of Thrombosis

خطوات
Platelets
تصلب
microscopic

-platelets come in contact with endothelium →
endothelial activation

Endothelial injury

- **Trauma** : surgical trauma – ligation
- **Inflammations**: arteritis – phlebitis – endocarditis
- **Diseases** : Atherosclerosis, M.I.



Virchow's Triad

Altered blood flow

- **General stasis**: H.F. – prolonged bed rest
- **Local stasis**: Dilated chambers – Aneurism – Varicose vein
Hyperviscosity (polycythemia & Sickle cell) Usually in small vessels – leukemia
- **Turbulence**: Atherosclerosis - Bifurcations

- Prevents dilution of clotting factors
- Decreased flow of factors inhibitors

Hypercoagulability

- **Acquired**:
Prolonged bed rest
Pregnancy & Hyperestrogenism
Post operative or burns
Pancreatic & Prostatic cancer
Post traumatic (accidents)
- **Genetic**: Inherited protein S, or factor V, or factor II (prothrombin) mutation

Mechanisms of Thrombosis

Endothelial injury:

○ Adhesion of platelets

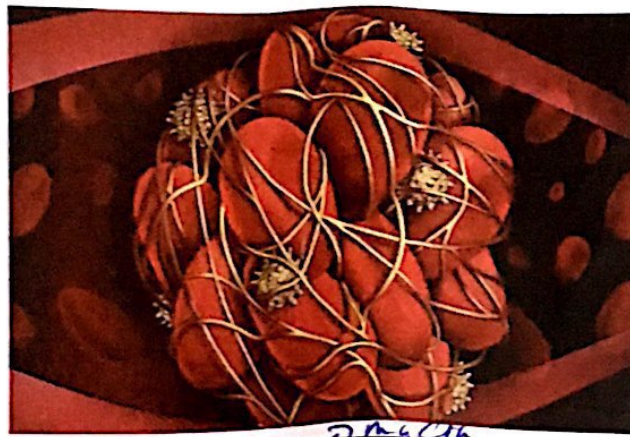
- Endothelial injury → Release of coagulation factor VIII (Von Willbrand)
- Factor VIII acts as a bridge → adhesion of platelets to collagen of B.V.
- Platelets are arranged in ridges (lines of Zahn): homogenous basophilic (platelets provide firmness to thrombus)

○ Activation of intrinsic pathway → activation of Fibrinogen → fibrin

- Fibrin deposition between lines of Zahn
- RBCs & WBCs may be seen trapped within fibrin

○ Release of Tissue factor → extrinsic pathway → excess fibrin deposition

○ Depletion of Prostacyclin (anti platelet) & Plasminogen activator (fibrinolytic)



- In Cancers → secretion of procoagulants → hypercoagulability
- In pregnancy & contraceptive pills → excess estrogen → Liver secrete → coagulation factors & decreases Prothrombin III → Hypercoagulability
Venous congestion in lower limb during pregnancy
- Old age → decreased PGI2, increased platelet aggregation
- In SLE → antiphospholipid → decreased PGI2, increased platelet aggregation + protein C

Morphology of thrombus

- Pale thrombus In Arteries or cardiac - Firm - (contain platelets and fibrin)
- Red thrombus In complete occlusion - Soft gelatinous - (more RBCs-less platelets)
- Mixed thrombus In veins
- Septic Bulky - yellowish (containing bacteria, septic emboli → pyemia)

Sites

Venous Thrombosis

the most common

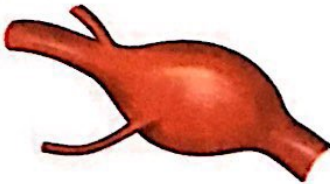


	Phelebo-Thrombosis	Thrombo-Phelebitis
Def	Thrombosis in <u>non</u> -inflamed veins	Thrombosis in <u>inflamed</u> veins
Causes	Stasis or H.F. Hypercoagulability (enumerate.)	Infection (Septic thrombo-phelebitis) Radiation, trauma, chemicals
Sites	- Superficial (saphenous) with varicose vein - Deep Venous Thrombosis DVT (calf, iliofemoral)	Inflamed veins of nearby infection e.g. Appendicitis, puerperal sepsis
Fate	-Superficial → Thrombus propagation -DVT → Pulmonary Embolism	-Septic → Pyemia

Migratory Thrombophlebitis: Recurrent thrombosis in different veins in case of cancer Pancreas (Trousseau's syndrome)

Arterial Thrombosis

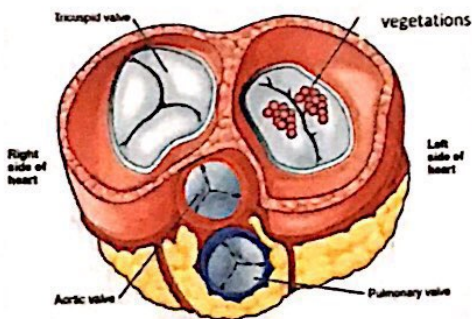
Arteritis, e.g. PAN- **A**neurism - **A**therosclerosis
common in **coronaries**, **cerebral** at site of bifurcations



Capillary Thrombosis

DIC - Vasculitis - acute inflammation

Cardiac Thrombosis



1. **Atrial Ball -valve:** in atrial dilatation with M.S. (free in the lumen or plug the valve)
2. **Atrial Mural:** attached to endocardial surface
3. **Vegetations (on cardiac valves):** diseased valve e.g. Rheumatic endocarditis, hypercoagulability
4. **Ventricular Mural:** On top of Myocardial infarction
5. **Agonal** inside right ventricle & pulmonary at the time of death

Fate and complications of Thrombosis

- **Small recent thrombus** → Dissolution (by fibrinolytic system)

N.B. fibrinolytics are useful in recent thrombi only. Old ones with extensive fibrin are resistant.

- Occluding or old thrombi:
 - **Organization**: heal by GT formation inside blood vessel → scar retraction and blood flow is restored.
 - **Canalization**: canal is open inside organized thrombus
 - **Calcification 'dystrophic'**: (phlebolith) detected by x-ray
 - **Embolization**: Septic → pyemia, Aseptic → ischemia, infarction
 - **Complication**:
 - Arterial: ischemia, infarction, gangrene
 - Venous: congestion, edema
- **Propagation**: in small arteries, and veins, multiple **clots** on top of multiple **thrombi** → propagation → reach the right side of the heart

D.I.C.

Disseminated intravascular coagulation: widespread thrombi in multiple vessels with associated bleeding tendency

Causes:

Thrombotic factor (T) → Obstetric complications (e.g. missed abortion)

- Cancers
- Septicemia

Pathogenesis:

Activated coagulation system → multiple thrombi in blood → consumption of platelets & fibrinogen → Bleeding tendency with activation of fibrinolytic system → small microscopic thrombi in microcirculation

Complications:

- Ischemic infarctions in multiple organs (Brain – Renal – Lung)
- Fatal Bleeding

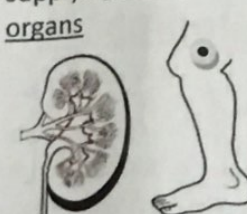


thrombus - embolus

Embolism

Embolus is a circulating, insoluble solid, liquid or gas. Embolism is impaction of embolus
embolism is seen in small arteries or portal vein branches

Thrombo-Embolism (Detached thrombus)

	Pulmonary Embolism	Arterial embolism	Paradoxical embolism	Septic
Origin Of thrombus	Venous -Systemic <u>veins</u> (DVT) -Rt. side of the heart	Arterial - <u>Arteries</u> (3 A ?) -Cardiac from left side (vegetations, Mural)	Venous Systemic <u>veins</u>	Venous Infamed <u>Veins</u> Septic thrombophlebitis
Fate	Embolism of <u>pulmonary</u> artery or its braches 	Embolism of arteries supplying <u>limbs</u> or <u>organs</u> 	Embolism of arteries supplying <u>limbs</u> or <u>organs</u> (?) <i>(embolus reach right side of the heart then pass to left side through ASD, VSD)</i>	Lung or Liver 
Effect	- <u>very Small</u> emboli → organization (fibrous web) - <u>Small</u> size → 1-lung <u>infarction</u> (if the lung is congested) 2-or ruptured branch → <u>hemorrhage</u> 3-Or multiple emboli → <u>pulmonary</u> <u>hypertension</u> & Rt. S. H.F. - <u>Large</u> Saddle embolus → occlude >60% of pulmonary trunk → Acute heart failure → <u>Sudden</u> <u>death</u> in minutes Death due to heart failure & serotonin in thrombus	(if the collaterals are not sufficient) -Organ ischemia → infarction -Limb ischemia → gangrene	(if the collaterals are not sufficient) -Organ ischemia → infarction → gangrene -Limb ischemia → pale, pulsless, and cold	Portal Pyemia Pulmonary pyemia Systemic pyemia

Acute
RT Side
Heart
Failure

Fat embolism

Aetiology:

- Fracture of long bone
- Severe trauma of subcutaneous fat or burns

Pathogenesis: shortly within 1-3 days in 1% of cases:

- Fat globules → emboli in veins → reach pulmonary → mechanical obstruction →
Dyspnea
- Brain → irritability B.M. → depression
- 10% → Fatal

Amniotic fluid embolism

Aetiology:

- Vigorous uterine contractions during labor. In 1/50000 delivery

Pathogenesis:

- Amniotic emboli in injured uterine veins → reach pulmonary artery → mediators → **Pulmonary spasm** → **Acute right sided H. F. (fatal)**
- Chemicals in Amniotic fluid → **DIC** → severe bleeding



Air embolism

Aetiology:

- Accidental: Injury of neck veins – injury chest veins – tubal insufflation
- Decompression sickness (caisson disease)
>100cc → large bubbles → right ventricular failure

Pathogenesis of Caisson disease:

- During deep diving → high pressure → nitrogen gas dissolve in blood
- Sudden release of pressure → gas is forming bubbles in blood
- Gas bubbles → Dyspnea, muscle and joint ischemia (bends)
(treated by forced pressure, then gradual decompression in specialized room)



Tumor emboli (metastasis)

Parasitic emboli

- ova of *Shistosoma* → periportal fibrosis
- Larva of *Hydatid* → liver Cyst
- Ameoba → Amoebic Liver Absces

DIC ← Thrombogenic factor Amnion fluid
 ↓
 Coagulation compounds
 ↓
 Vasoconstrictor factor
 ↓
 Death ← Pulmonary Regm

Ischemia

Decreased arterial blood supply

	Acute Sudden/ complete occlusion	Chronic Gradual/ partial occlusion
Causes	- <u>Outside</u> : <u>Ligation</u> , twisting, compression - <u>Vessel wall</u> : <u>Complicated atheroma</u> (hemorrhage) – spasm (Reynaud's disease) – ergot poisoning - <u>Lumen</u> : <u>Thrombus</u> – <u>embolus</u>	<u>Atherosclerosis</u> <u>Arteritis</u> <u>Arteriosclerosis</u> (in hypertension)
effect	Infarction In case of : -Organs with <u>end arteries</u> (retina, coronary, spleen, mesenteric, cerebral, renal) - <u>Rapid</u> occlusion -Tissue with <u>low vulnerability to hypoxia</u> (brain: 3 min, Heart: 30 min) -General Hypoxia (anemia, H.F.)	<i>If collaterals are insufficient</i> Atrophy & fibrosis Pain & claudications (accumulated metabolites) Infarction (in case of severe hypoxia)

Infarction

Coagulative necrosis of tissue due to arterial or venous occlusion. Liquifactive necrosis in CNS.

Causes of infarction: causes of acute ischemia (enumerate)

Gross picture of infarction:

Aseptic

- **Shape** : wedge, pyramidal (*Distal base, proximal apex*)
- **Surface(base)**: Bulging then → Retraction (*later fibrosis*)
- **Color**:
 - **Pale** (*in solid organs : Heart, spleen, kidney*)
 - **Red** (*Intestine, Lung, gonads*) because of dual blood supply, Loose tissue, & congestion just before necrosis
- **Borders**: Hyperemic (Acute inflammation)
- **Covering serous sac** : Thick opaque (Fibrinous inflammation)



Septic (caused by septic emboli – or infection of infarction)

- Yellowish foci – surrounded by zone of congestion

Microscopic picture of infarction:

- Picture of **Coagulative necrosis** (describe?) → surrounded by inflammation
- In Brain infarction → microglia filled with fat (granular corpuscle)

Fate of infarction: -Healed infarction → fibrosis (gliosis in brain).

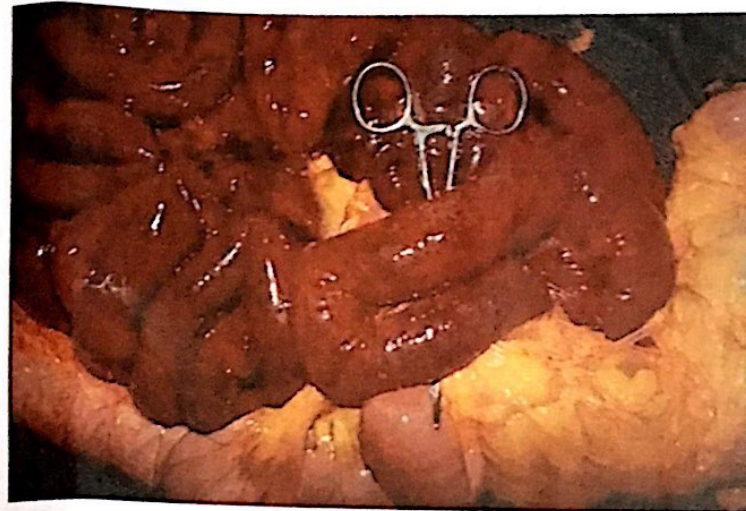
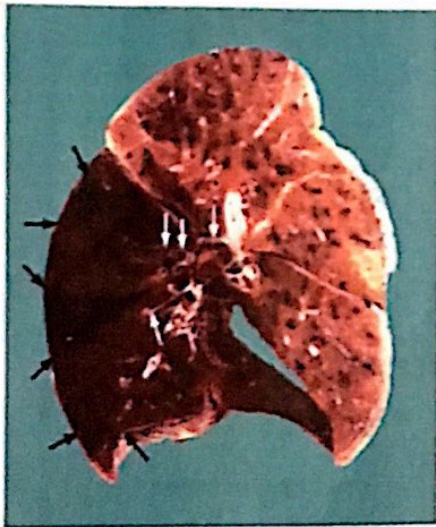
Clinical effects:

- Fever, Leukocytosis, elevated **ESR** (?)
 - Elevated serum enzymes : Transaminases , CK (In M.I.)
 - Cerebral: damage of pyramidal tract → **hemiplegia**
 - M.I. : **Arrhythmia** → cardiogenic shock , Fibrosis → **H.F.**
 - Lung: **Hemoptysis** (due to congestion) – **Chest pain** (due to pleurisy)
 - Intestinal: **Obstruction** – **gangrene** & toxemia – Abdominal pain (peritonitis)
 - Renal: **Hematuria** – **Senile** atherosclerotic kidney (repeated infarctions)
- Renal infarction is painless, because renal capsule is innervated by different nerve fibers.*

different blood supply

N.B. Infarction of solid organs is pale, because they are supplied by terminal arteries, and solidity limits spread of hemorrhage from ruptured vessels

Lung & intestinal infarction (red infarction)



MCQ

1-All the following are possible causes of osmotic edema EXCEPT:

- a) Liver failure
- b) Nephritic syndrome
- c) Hypoproteinemia
- d) Protein-losing enteropathies

2-Lymphatic edema is:

- a) Generalized
- b) Induced by Thrombosis
- c) Non pitting
- d) Always reversible

3-All the following mechanisms are included in cardiac edema EXCEPT:

- a) Salt and water retention
- b) Increased hydrostatic pressure
- c) Increased permeability
- d) Decreased osmotic pressure

4-All the following causes may lead to Generalized edema EXCEPT:

- a) Left sided heart failure
- b) Right sided heart failure
- c) Severe proteinuria
- d) Radical mastectomy with axillary dissection

5- Congestion is:

- a) caused by arterial dilatation
- b) Caused by atherosclerosis
- c) Passive accumulation of blood
- d) All of the above

6- Nutmeg liver appearance is due to:

- a) Liver cirrhosis
- b) Fatty changes & congestion
- c) Hemosiderin & fibrosis
- d) All of the above

7- In Splenic congestion:

- a) Red pulp is atrophic
- b) White pulp is proliferated
- c) White pulp is atrophic
- d) All of the above

8- "Brown induration" is a result of:

- a) Pulmonary edema
- b) right sided heart failure
- c) Left sided heart failure
- d) none of the above

9- Which of the following diseases may lead to Hematuria?

- a) Malignant hypertension
- b) Vitamin K deficiency
- c) Thrombocytopenia
- d) all of the above

10- All of the following diseases presents with melena EXCEPT:

- a) Bleeding peptic ulcer
- b) Piles
- c) Ruptured varices
- d) both a&c

MCQ

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- c) Hypoproteinemia
- d) Protein-losing enteropathies

2-Lymphatic edema is:

- a) Generalized
- b) Induced by Thrombosis
- c) Non pitting
- d) Always reversible

3-All the following mechanisms are included in cardiac edema EXCEPT:

- a) Salt and water retention
- b) Increased hydrostatic pressure
- c) Increased permeability
- d) Decreased osmotic pressure

4-All the following causes may lead to Generalized edema EXCEPT:

- a) Left sided heart failure
- b) Right sided heart failure
- c) Severe proteinuria
- d) Radical mastectomy with axillary dissection

5- Congestion is:

- a) caused by arterial dilatation
- b) Caused by atherosclerosis
- c) Passive accumulation of blood
- d) All of the above

6- Nutmeg liver appearance is due to:

- a) Liver cirrhosis
- b) Fatty changes & congestion
- c) Hemosiderin & fibrosis
- d) All of the above

7- In Splenic congestion:

- a) Red pulp is atrophic
- b) White pulp is proliferated
- c) White pulp is atrophic
- d) All of the above

8- "Brown induration" is a result of:

- a) Pulmonary edema
- b) right sided heart failure
- c) Left sided heart failure
- d) none of the above

9- Which of the following diseases may lead to Hematuria?

- a) Malignant hypertension
- b) Vitamin K deficiency
- c) Thrombocytopenia
- d) all of the above

10- All of the following diseases presents with melena EXCEPT:

- a) Bleeding peptic ulcer
- b) Piles
- c) Ruptured varices
- d) both a&c

11- All of the following signs are seen in septic shock EXCEPT:

- a) Tachycardia
- b) Tachypnea
- c) Cold & wet skin
- d) Low blood pressure

12- Which postmortem finding is seen after shock:

- a) Adrenal depletion
- b) Cerebral edema
- c) Visceral hemorrhage
- d) All of the above

13- All the following features are found in Clot EXCEPT:

- a) lines of Zahn
- b) Devoid of platelets
- c) Blood is stagnant
- d) Found outside CVS

14- Which of the following situations lead to Thrombus formation:

- a) Polycythemia
- b) Portal hypertension
- c) Heart failure
- d) All of the above

15- Which factor is essential for formation of Irreversible thrombus:

- a) Factor VIII
- b) Thromboplastin
- c) ADP & Thromboxan
- d) non of the above

16- The number of propagating thrombi could be anatomically calculated as follow:

- a) Number of tributaries
- b) Number of related arteries
- c) Number of tributaries + 1
- d) Number of tributaries - 1

17- Features of arterial thrombus:

- a) Caused by prolonged bed rest
- b) Always red
- c) Grows against direction of flow
- d) all of the above

18- Agonal thrombus is formed inside:

- a) veins during death
- b) Left ventricle
- c) right ventricle and pulmonary
- d) systemic arteries

19- Features of DIC:

- a) Bleeding tendency
- b) Ischemic infarctions
- c) Platelet & fibrinogen deficiency
- d) All of the above

20- Thrombus which was formed in systemic veins and ends by cerebral infarction:

- a) Pulmonary embolism
- b) Thrombophlebitis
- c) Paradoxical embolism
- d) Atherosclerotic plaque

21- After a period of hospitalization following a car accident, the patient noticed swollen & tender calf. Short after, a sudden chest pain & dyspnea develops:

- a) Fat embolism
- b) Thromboembolism
- c) Arterial thrombosis
- d) Thrombophlebitis

22- Amniotic fluid emboli lead to:

- a) Pulmonary Vasospasm
- b) Massive uterine bleeding
- c) Chest pain
- d) All of the above

23- Caisson's disease is an example of:

- a) Pulmonary thromboembolism
- b) Systemic Thromboembolism
- c) Fat embolism
- d) none of the above

24- Red infarction is seen in:

- a) Heart
- b) Kidney
- c) Lung
- d) none of the above

25- Examples of moist gangrene include all of the following EXCEPT:

- a) Gangrene following Strangulated hernia
- b) Diabetic gangrene
- c) Crushing limb injury
- d) Atherosclerotic limb

26- All the following features are found in Moist gangrene of limb EXCEPT :

- a) Putrefaction
- b) Line of separation
- c) Toxemia
- d) Ischemia

27- Reynaud disease is characterized by:

- a) Arterial vasospasm
- b) aggravated by cold
- c) Cyanosis of extremities
- d) all of the above

28- Gas gangrene of the deep wound occurs in the presence of:

- a) Arterial ischemia
- b) Venous occlusion
- c) Anaerobic Clostridia
- d) Aerobic bacteria

29- Black color of gangrene is due to:

- a) Hemosiderin
- b) H_2S
- c) Iron Sulphide
- d) Tissue necrosis

30- Generalized edema results from all of the following, EXCEPT:

- a) Systemic hypertension
- b) Congestive heart failure
- c) Cirrhosis
- d) Hyperaldosteronism

31- Embolism occurs in:

- a) Bilharziasis
- b) Leukemia
- c) Bone fracture
- d) All of the above

32- All are characteristic of dry gangrene EXCEPT:

- a) Slow progression
- b) Marked toxemia
- c) Black discoloration
- d) Self separation may occur

33- In Chronic venous congestion of the lung, alveoli show all ,EXCEPT:

- a) Heart failure cells
- b) RBCs
- c) Transudate
- d) Exudate

34- Thrombosis is more common in:

- a) Veins
- b) Arteries
- c) Cardiac valves
- d) Left atrium

35- A thrombus over myocardial infarction is called:

- a) Ball thrombus
- b) Mural thrombus
- c) Vegetation
- d) none of the above

36- The following are factors enhancing Venous thrombosis EXCEPT:

- a) Endothelial damage
- b) Stasis
- c) Increased fibrinogen
- d) Decreased plasma proteins

37- The effect of embolus depends on:

- a) Collaterals
- b) Infection of embolus
- c) Size of embolus
- d) All of the above

38- Which type of shock is associated with massive pulmonary embolism:

- a) Hypovolemic
- b) Cardiogenic
- c) Neurogenic
- d) none of the above

39- All the following leads to arterial thrombosis EXCEPT:

- a) Thrombangitis obliterans (Buerger)
- b) Poly arteritis nodosa
- c) Atherosclerosis
- d) Heart failure

40- The most common origin of pulmonary emboli is:

- a) DVT
- b) Varicose veins
- c) Cardiac diseases
- d) Valve diseases

Q6: Which of the following can cause generalized pitting edema

- a) Infiltration of superficial lymphatics by cancer cells in a cancer breast
- b) Liver disease
- c) Lymph node resection in breast cancer
- d) Elephantiasis
- e) Deep vein thrombosis

Q7: Which of the following is a cause of localized edema

- a) Severe malnutrition
- b) Nephrotic syndrome
- c) Right ventricular failure
- d) Abscess

Q8: A 55-year-old male presents with coronary thrombosis left ventricular wall infarction occurs. 24 hours later, he develops dyspnea. The most likely microscopic findings are:

- a) Pulmonary capillary congestion and intra alveolar exudate
- b) Necrotic alveolar walls
- c) Congested pulmonary capillaries and intra alveolar transudate
- d) Alveolar wall fibrosis and hemosidrin laden macrophages

Q9: A 50-year-old male developed an arterial thrombus. One of the following is true

- a) The main effect is congestion distal to obstruction
- b) The thrombus is dark red in color
- c) Endothelial injury may be involved in its formation
- d) It is known as phlebothrombosis

Q10: Infarcts tend to pale when they occur in:

- a) Intestine
- b) Spleen
- c) Lung of a patient with left side heart failure
- d) Torsion testis

Easy Pathology

Dr. Abdelrahman Khalifa



Neoplasia part 1

Ainshams 2018 - 2019

Neoplasia

Mass of cells, with uncontrolled, irreversible & unlimited proliferation

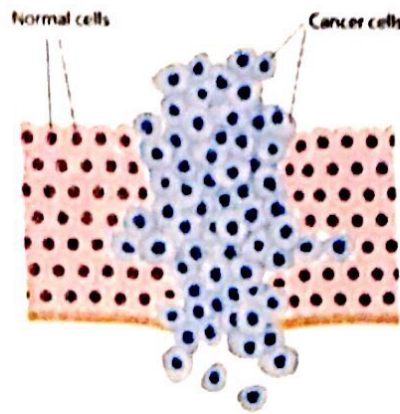
Classifications:

According to Behavior:

- Benign
- Malignant

According to Origin:

- Epithelial
- Mesenchymal
- Others



Microscopic features:

• Structure:

○ Parenchyma

- Epithelial tumors: acini, papillae, sheets, or cords
- mesenchymal tumors: Bundles, whorls with matrix (e.g. cartilage)
- some tumors show mixed pattern (e.g. pleomorphic adenoma, fibroadenoma, carcinosarcoma)

○ Stroma formed of:

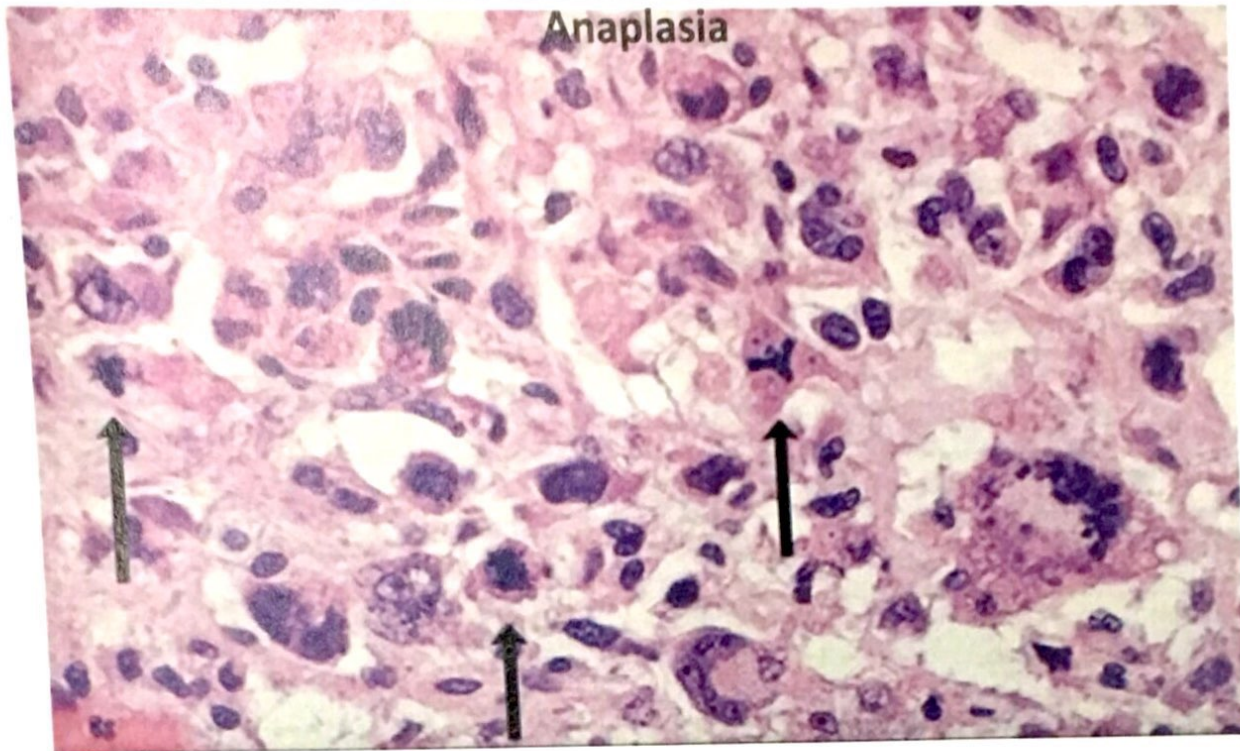
- Collagenous fibrous tissue
 - Stimulated by b-FGF
 - Scant stroma → gives fleshy consistency (e.g. sarcoma)
 - Excess (desmoplasia) → firm gritty (e.g. scirrhous carcinoma)
- Blood vessels (newly formed by Angiogenesis from preexisting ones)

- **Differentiation** similarity to origin. Variable according to type benign or malignant differentiation is defined as the extent of morphological and functional resemblance of parenchymal tumor cells to normal cells

- **Anaplasia** loss of differentiation, with morphological abnormality

- **Pleomorphism** variable shape & size of tumor cells
- **Hyperchromatism** dark stained (increased nucleoprotein)
- **Increased N/C ratio** > 1:4
- **Frequent mitoses & Abnormal mitotic figures** (tripolar, multipolar)
- **Abnormal nuclei (Anisonucleosis)** vesicular, pleomorphic
- **Prominent & multiple nucleoli**
- **Tumor giant cells** (large cells, with multiple bizarre nuclei)
- **Loss of polarity** disturbed orientation and arrangement
- **Functional Changes** (better differentiated tumors secrete hormone, bile or keratin)
- **Chromosomal changes** (mutated genes & increased number of chromosomes → large nucleus)
e.g. Philadelphia chromosome in Chronic myeloid Leukemia

- **Inflammatory reaction** caused by 2ry infection of ulcer - or immune reaction against tumor (e.g. Inflammatory cells in Seminoma)
inflammatory reaction : chronic inflammation or granuloma



Dysplasia

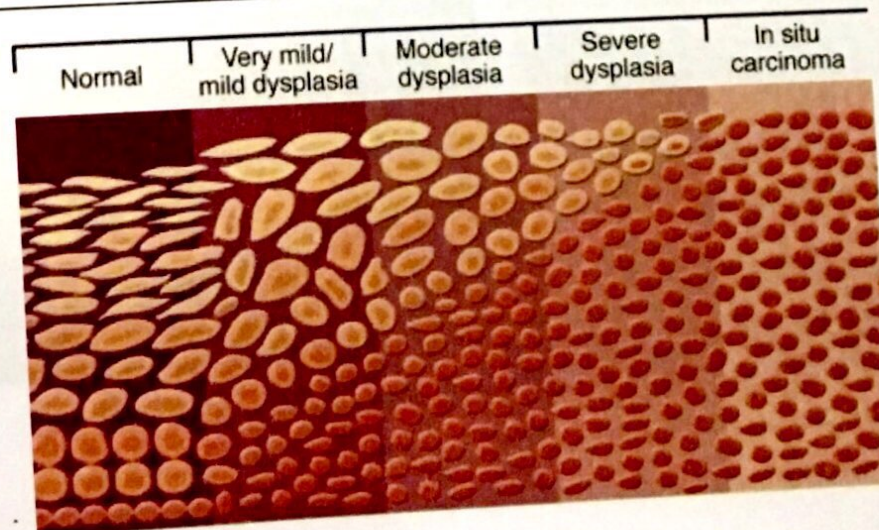
Disordered proliferation **arrangement** and **morphology** of cells but not neoplastic Site surface epithelium and glands. caused by chronic irritation (e.g. prolonged inflammation)

Microscopic changes : disorder of arrangement + Anaplasia (enumerate)

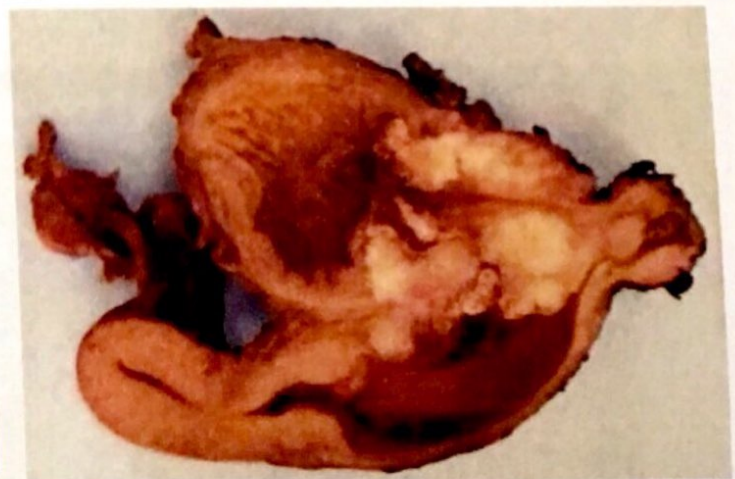
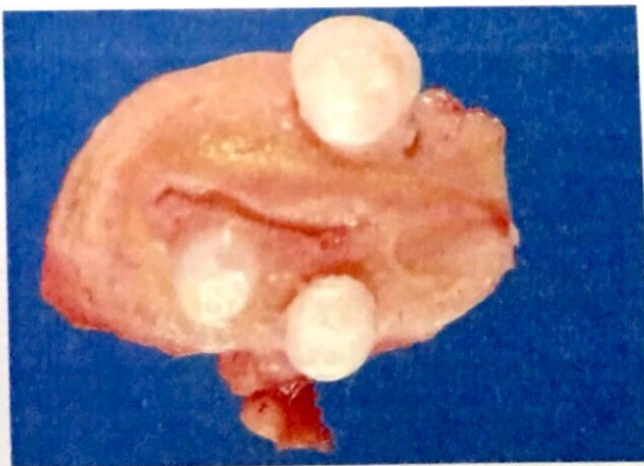
Grades of dysplasia in Stratified Squamous epithelium:

- **Grade I (mild)** : dysplasia of the lower third (reversible)
- **Grade II (moderate)** : dysplasia of the lower 2/3 (reversible)
- **Grade III (severe)** : dysplasia of the full thickness → may change to Carcinoma in situ (CIS) not invading basement membrane

Fate: Dysplasia is precancerous but reversible



	Benign tumors	Malignant tumors
Behaviour	Rate of growth Slow (could be <u>rapid</u> in <u>Leiomyoma</u> , which is hormonal-dependant) some tumors may <u>shrink</u> suddenly due to ischemia e.g. <u>pituitary adenoma</u>	Fast <u>Lead to central ischemic necrosis</u> -but Some tumors may shrink & disappear due to host immunity (e.g. <u>melanoma</u> , <u>choriocarcinoma</u>)
	Mode of growth Expansion	Invasion and destruction
	Effect Compression – obstruction – hormonal secretion	Same..... + effects of metastasis
	Spread & metastasis Absent	present
	Recurrence Not recurrent	Recurrent (<i>why?</i>)
	Prognosis Good prognosis	Bad prognosis
Gross	Shape & boundaries In solid organs: Rounded – oval surface epith.: papillae - polyp	In solid organs: irregular ill-defined surface epith.: fungating – ulcer- diffuse thickening
	Capsule Capsulated Except <u>leiomyoma</u> , well-demarcated by compressed tissue (false capsule)	Not capsulated Some are partially capsulated (e.g. <u>follicular carcinoma</u> of thyroid)
	Surrounding tissue compressed	infiltrated
Micro	Differentiation Well differentiated	Variable well, moderate, poor, or undifferentiated
	Anaplasia Absent	Present
	Chromosomal changes Infrequent	Present



The most important feature of malignancy is **Invasion & metastasis**

		Carcinoma	Sarcoma
origin		epithelial	mesenchymal
Behaviour	Rate of growth	Less Rapid	Rapid
	Mode of growth	infiltration	Infiltration and Expansion
	Spread	Early lymphatic → late blood	Early blood spread
	Prognosis	Relatively better	worse
	incidence	More common	Less common
	Age	Old age	Young age
Gross	Size	Relatively Smaller	Large bulky mass
	Shape	In solid organs: irregular ill-defined surface epith. : fungating – ulcer-diffuse thickening	irregular ill-defined
	C/S	Grayish white (better stroma) Less necrosis and hemorrhage.	Homogenous with extensive necrosis and hge.
	Consistency	Firm	Soft fleshy
Micro	Differentiation	More	Less
	Cohesion	More cohesive Arranged in sheets, glands, cords Separated by stroma, or papillae	Less cohesive Highly cellular Individual cells
	Anaplasia	present	more
	Stroma	Less vascular Well formed fibrous stroma	highly vascular scant fibrous stroma

N.B. Malignant ulcer :

Raised everted edge – Necrotic hemorrhagic floor – Fixed indurated base



Methods of spread of Malignant tumors

- Benign tumor, Locally malignant tumors , & malignant brain tumors → No spread
- The more Anaplasia & tumor size → more likely is the spread
- 30% of malignant tumors → evident metastasis & 20% → occult metastasis

Lymphatic spread *(more common in carcinomas)*

	Lymphatic permeation	Lymphatic Embolism
mechanism	Proliferation of tumor cells <u>inside lymph vessel</u> as a cord	movement of tumor emboli by lymph vessels into <u>lymph nodes</u> → found <u>subcapsular</u> → then destroy L.N.
Effects	-Lymphatic edema - Retrograde lymphatic spread (GIT & prostatic carcinoma → reach supra clav L.N. <u>Virchow's L.N.</u>)	-Regional LN: <u>large, firm, fixed</u> -Spread to other LNs -Late blood spread (?)

- L.N. enlargement in tumor is due to metastasis or Reactive Lymphadenitis and histiocytosis caused by cancer products.
- GIT and some breast carcinomas → reach both ovaries by lymphatics Krukenberg tumor
- **Sentinel L.N.** is the 1st L.N. receiving metastasis in regional L.N.

Hematogenous spread *(early in sarcomas)*

Mechanism:

- **Direct invasion** of blood vessels (mostly veins) → tumor emboli covered by platelets as a thrombus → reach distant site → early blood spread (common in **sarcoma**) .
Invasion of arteries is rare because of thick wall and elastic lamina
- **Lymphatic spread** → late blood spread (**carcinoma**)
- Some **carcinomas** invade blood vessels: Thyroid, HCC, RCC, prostatic
Renal cell carcinoma often invades renal vein to inferior vena cava

Common Sites of metastasis:

- **Lung** Receive metastasis from tumors drained by systemic veins e.g. RCC invades renal vein → inferior vena cava → right side of the heart
- **Liver** Receive metastasis from organs drained by portal vein (GIT)
- **Bone & Brain**

Organ Tropism

- Arrest of tumor emboli in vessels of specific organs by binding between adhesion molecules of tumor cells and specific receptors on target endothelium
- Thyroid, Lung, breast, renal, & prostatic carcinomas → bone metastasis
- Sarcomas → bone, Liver and Lung metastasis
- Bronchial carcinoma → Brain, liver and adrenal metastasis
- Seminoma & RCC → Lung metastasis



spleen ,heart & skeletal muscles do **not allow** tumor metastasis to grow

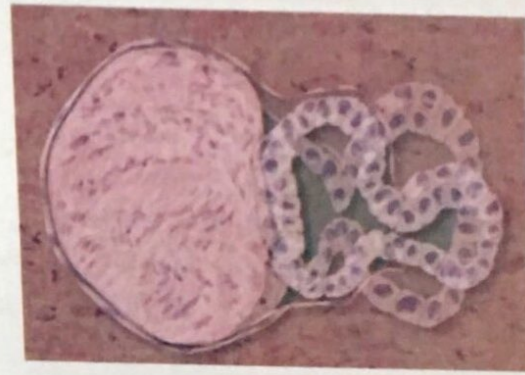
Spread through body cavities

- Serous sac : e.g. ovarian tumors → peritoneal , mesothelioma → pleural
- CSF : e.g. medulloblastoma → implanted in meninges

Perineural

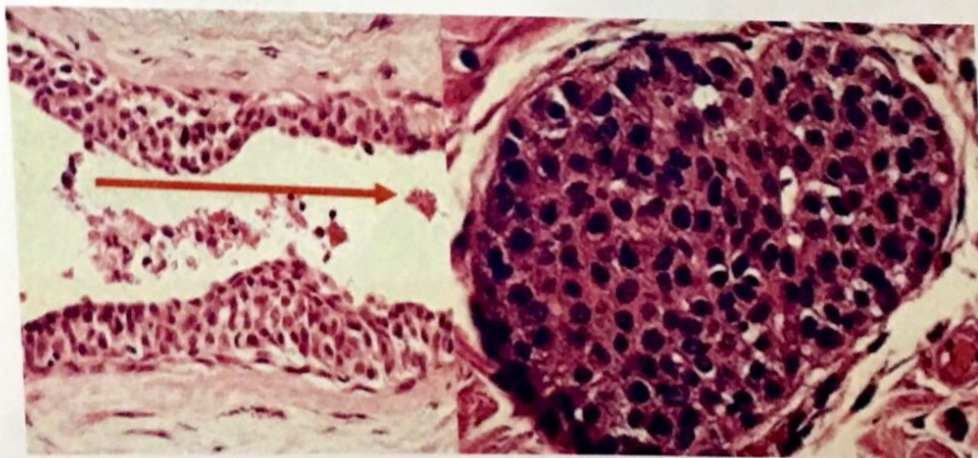
Prostatic, Pancreatic, and Parotid adenoid cystic carcinoma → secrete **MMPs** → invade nerve → Pain. Poor prognosis

Direction of growth is controlled by Growth factors secreted by tumor (towards the weakest point)



Intraepithelial

- **Duct carcinoma** may reach lobules through ducts
- **Endometrial carcinoma** reach ovaries through Fallopian tube
- **Renal Cell Carcinoma** reach urinary tract through ureter



Epithelial Tumors

Papilloma

Benign tumor of surface epithelium

Gross: papillae (*pedunculated – sessile*) - Single or multiple branching

Micro:

- **Core:** vascular fibrous tissue
- **Covered:** by proliferated epithelium
 - Squamous Cell Papilloma → covered by str. Squamous epith
 - Transitional Cell Papilloma → transitional
 - Columnar Cell Papilloma → columnar



Complications ulceration → bleeding & 2ry infection . Malignant transformation

Adenoma

Benign tumor of glandular epithelium

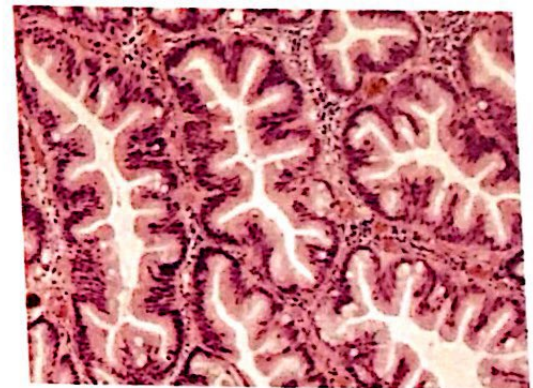
Sites

- Glands (*endocrine – exocrine*) : breast, thyroid, ovary, salivary...etc.
- GIT : Gastric ,intestinal, colonic & bronchi

Gross

- Capsulated well defined in solid organs
- Polyp in GIT
- Cystic containing secretion, or papillary cystic

Micro: glandular tissue & stroma



Complications

- Secretion of hormones (*e.g. thyroid adenoma*)
- Malignant transformation (*GIT adenomas are precancerous*)

Squamous cell carcinoma SCC

Malignant tumor of stratified Squamous epithelium

Sites: str. Sq. epithelium (*enumerate?*) - On top of squamous metaplasia

Gross:

Fungating, Ulcer: inverted edge , necrotic floor ,hard base, **infiltrating**

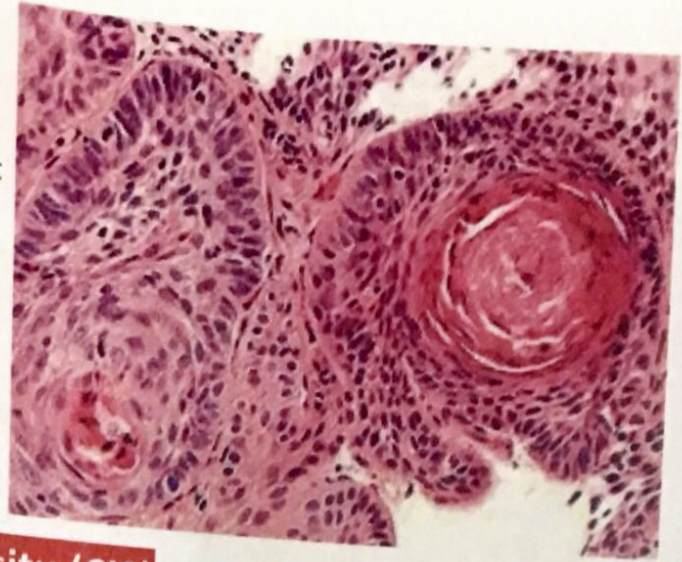
Micro:

- masses of malignant str. Sq. epith.
- variable in shape and size
- may show keratinized nests
- separated by stroma



Broder's grading:

- **Grade I:** 50% - 100% of masses → cell nest
- **Grade II:** 25% - 50% of masses → cell nest
- **Grade III:** less than 25% of masses → cell nest
- **Grade IV:** no cell nest



Carcinoma in situ (CIS)

Malignant epithelial changes, before invasion of basement membrane

Sites: glandular & surface epithelium: e.g. Breast, Bladder, Bronchi, Cervix, Skin... etc.

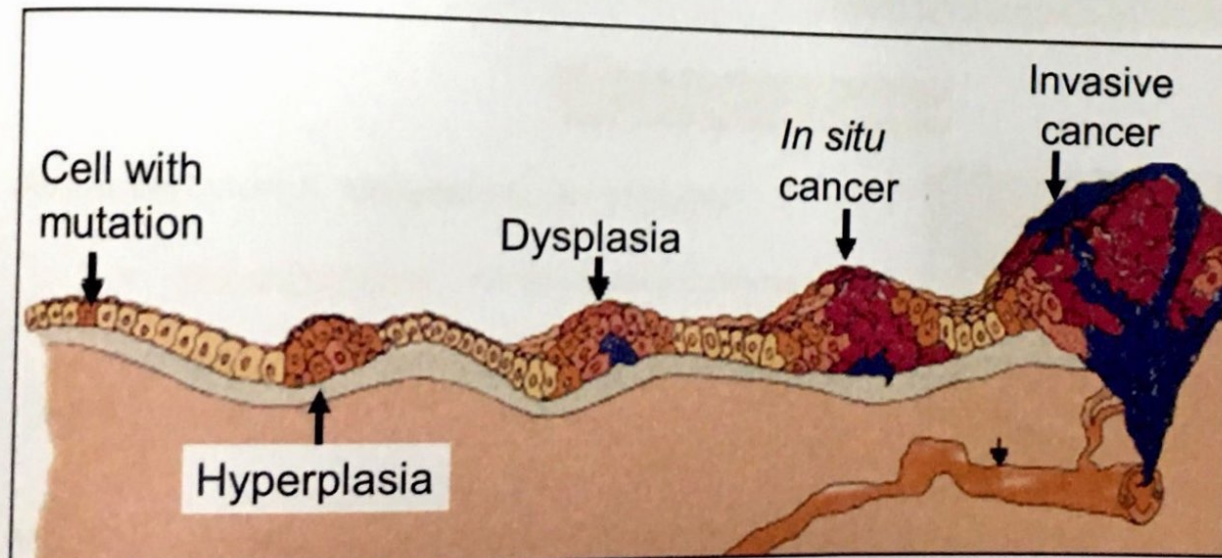
Micro:

Anaplasia (enumerate..?)

Loss of polarity (i.e. irregular arrangement of cells)

Basement membrane is intact

Fate: Invasive Carcinoma *after few years*



Basal cell carcinoma

Locally malignant 'Rodent ulcer' (the most common malignant of skin)

Sites: Skin (**upper part of the face**, around the eye), neck, back, shoulder, hands
the commonest site: above a line drawn from angle of mouth to ear lobule. (sun exposed)

P.F. U.V. rays, Arsenic, radiation, Fair white people, more in males

Gross:

- Red nodule (sometimes brown)
- Ulcer: inverted rolled in edge – necrotic floor – fixed base

Micro:

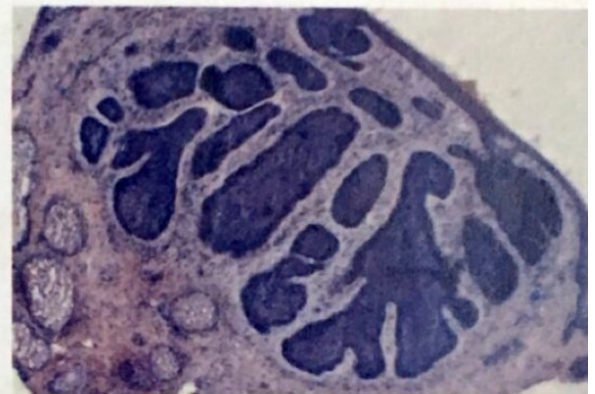
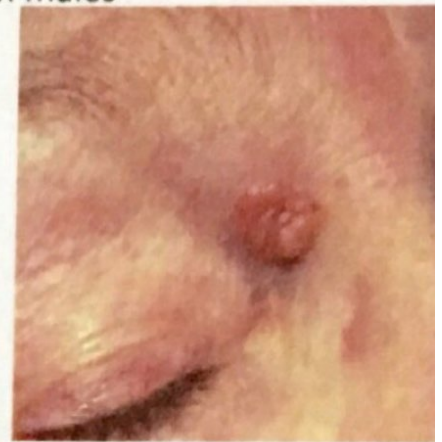
Malignant Cells with scant cytoplasm:

- Forming basaloid masses
- Peripheral pallisading
- Surrounded by stroma
- Melanin pigment

Complications

Local invasion

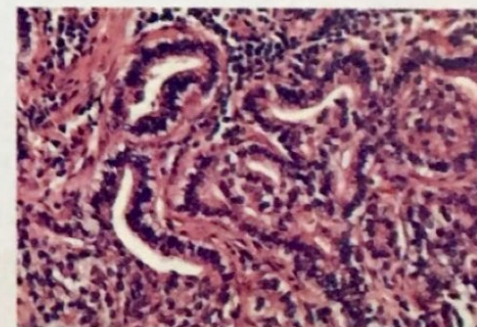
2ry infection of deep ulcers → lymphadenitis



Glandular-carcinoma

Adenocarcinoma 'Malignant tumor of glands'

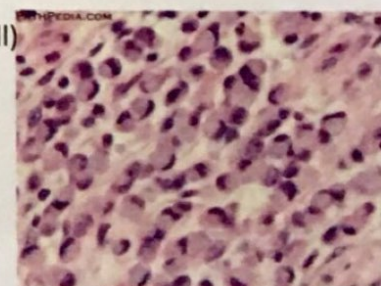
- Well deffrentiated : malignant **acini** & stroma
- Poorly differentiated : malignant cells, less **acini**



Mucoid : extracellular mucin lakes & malignant glands (e.g. colorectal carcinoma)

Signet ring: adeocarcinoma, with intracellular mucin (signet ring cell)

e.g. Gastric carcinoma & Krukenberg
 local spread is more aggressive



C.T. Tumors

Benign: e.g. Lipoma, fibroma

Gross: Capsulated well defined . micro: similar to origin

Malignant: Sarcomas

Haemangioma

The **most common** benign tumor

Sites: Subcutaneous – organs (e.g. liver)

Gross:

shape: irregular patch or swelling color: red, brown, blue

Micro:

- Vascular spaces lined with endothelium, containing RBCs
 - Small spaces in **Capillary hemangioma** (usually in skin)
 - Larger spaces in **Cavernous hemangioma** (skin < organs as liver and tongue)
- Fibrous stroma between vessels



Lymphangioma

tumor forming vascular spaces containing lymph

Sites: Head , neck (**Cystic hygroma** of newborn) , Submucous (lip, and tongue) – organs (e.g. liver, spleen)

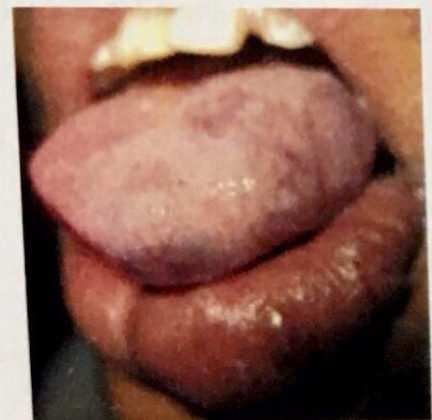
Gross:

shape: patch or swelling capsule: absent color: pale

Macro-glossia: enlarged tongue , **macro-chelia:** enlarged lips

Micro:

- Vascular spaces lined with flat endothelium, containing Lymph & lymphocytes
 - Small spaces in **Capillary lymphangioma**
 - Larger spaces in **Cavernous lymphangioma**
- Fibrous stroma between spaces



Nevus

Benign tumor of melanocytes

Gross: well defined Flat or elevated papule, brown or black

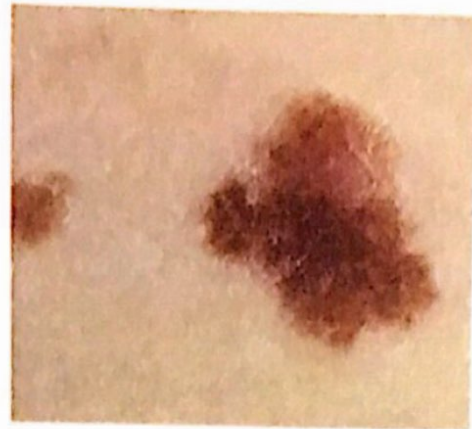
Microscopic Types: junctional – compound – intradermal

Melanoma

malignant tumor of melanocytes

Gross: nodule or malignant ulcer

Microscopic: malignant melanocytes, invading dermis
prognosis depends on depth of invasion



Teratoma

Composite tumor, forming ectodermal, mesodermal, and endodermal tissues, not related to site of origin

Origin: Totipotent stem cell

- Embryonic rests : present in midline & congenital
- Germ cell → gonadal & acquired

Types:

- **Mature (benign)** well differentiated mixed tissue
- **Immature (malignant)** immature fetal tissue
- **Mature with malignant transformation** (e.g. mature with squamous cell carcinoma or adenocarcinoma)
- **Mono-dermal** single type of mature tissue not related to site of origin
e.g. Struma-ovarii (normal thyroid tissue in ovary)



Embryonic tumors

Malignant tumor of embryonic tissue in children less than 5 years

Origin: Embryonic cells (partially differentiated cells)

Micro: Blastemal cells : small rounded or oval– dark nuclei

Types:

- Medulloblastoma (Cerebellum)
- Retinoblastoma (eye)
- Hepatoblastoma (liver)
- Neuroblastoma (adrenal medulla) **the most common**
- Nephroblastoma or Wilm's tumor (renal)



Hamartoma

Tumor-like mass of disorganized mature tissue

- Lung hamartoma: bronchi, vessels, and cartilage
- Liver hamartoma: Liver cells, bile ducts, & vessels

Choristoma (heterotopia): congenital ectopic tissue, e.g. pancreatic tissue in stomach

Locally malignant tumors

- Slower rate of growth
- Local invasion
- Rare distant spread
- Morphologically similar to malignant
- Better prognosis
- Includes:
 - Adenoma
 - Astrocytoma grade II
 - Basal cell carcinoma
 - Carcinoid
 - Desmoid tumor
 - Giant cell tumor (Osteoclastoma)

Grading of malignant tumor:

is microscopic evaluation of differentiation (similarity to origin), depends on similarity to origin and mitosis

I: well differentiated

II: moderately differentiated **III**: poorly diff. **IV**: undifferentiated

Staging of malignant tumor: is evaluation of extension and spread, which is much more important than grading, and requires clinical and radiological investigations. requires Radiology (CT, MRI, PET) + Clinical + pathological examination

TNM system

T: tumor size & extent, **N**: number of affected LNs, **M**: distant blood metastasis

Tis: CIS T1: <2cm T2: 2-5 cm T3: 5-10cm T4: >10 cm

N0: no LN mets. N1: regional LN N2: extensive regional LN mets. N3: distant LN mets.

M0: no distant spread M1: distant blood spread

1-Pigmented malignant ulcer in the face could be one of the following (Except)

- a-Melanoma
- b-Basal cell carcinoma
- c- Hemangioma
- d- none

2- Staging of malignant tumors evaluates :

- a-differentiation
- b-necrosis
- c- a&b
- d- tumor extension

3- Signet ring carcinoma is a type of:

- a-Squamous cell carcinoma
- b-Adenocarcinoma
- c- Anaplastic carcinoma
- d- none of the above

4-Hamartoma is:

- a-Mixed germ cell tumor
- b-Malignant
- c-Tumor like developmental abnormality
- d-Locally malignant

5-Krukenberg tumor is:

- A-Peritoneal sarcoma
- b-Benign ovarian tumor
- c- Gastric carcinoma
- d- all of the above

6-All are embryonic tumors (except):

- a-Nephroblastoma
- b-Hepatoblastoma
- c- Embryonal rhabdomyosarcoma
- d- Teratoma

7-Virchow's lymph node , all of the following are true (except):

- a-induced by lymphatic embolism
- b-Left supraclavicular
- c- Gastric carcinoma is the origin
- d- Enlarged and fixed

8-Sarcoma is :

- a-Malignant of epithelium
- b-common to form malignant ulcer
- c- Highly vascular
- d- Common below 6 years

9-The following feature is characteristic for Basal cell carcinoma :

- a-Keratinized nests
- b-Blood metastasis is common
- c- Pallisading
- d- Skin is not the only site of origin

10-All The following tumors send metastasis (Except):

- a-Gastric carcinoma
- b-Adamantinoma
- c- Broncheogenic carcinoma
- d- Squamous cell carcinoma

11-The following are complications of benign tumors (except):

- a-hormonal imbalance
- b-Obstruction of tubes
- c- Hepatic metastasis
- d- Compression of vital organs

12-Struma ovarii is an ovarian tumor showing:

- A-Metastatic thyroid tissue
- b-normal thyroid tissue
- c- Immature teratoma
- d- Hamartoma

13-Broder's grading of Squamous cell carcinoma depends on:

- A-Invasion
- b-Keratinized cell nests

c- Metastasis

d- Inflammation

14- The most reliable prognostic factor of melanoma:

A-Vertical thickness

b-Radial diameter

c- Darkness of color

d- Anaplasia

15- Which of the following lesions is locally malignant:

A-Giant cell tumor

b-Endometrial hyperplasia

c- Congenital nevus

d- Hemangioma

True/ False:

- 1- Stage T2 N2 M0 has better prognosis than stage T3 N0 M0
- 2- Spindle cell sarcoma is a well differentiated sarcoma
- 3- Teratoma is epithelial in origin
- 4- Carcinoma in situ has local invasion without distant metastasis
- 5- The commonest site of cystadenoma is the breast
- 6- Adenocarcinoma has better prognosis than mucoid carcinoma
- 7- Papilloma is a benign capsulated tumor
- 8- Desmoplasia is an extensive fibrous reaction inside tumor
- 9- Mucoid carcinoma has better prognosis than adenocarcinoma
- 10- Prostatic carcinoma is painful due to perineural invasion
- 11- Virchow's L.N. is a result of retrograde lymphatic permeation
- 12- Some malignant tumors may reach the brain without lung metastasis
- 13- Krukenberg tumor is a bilateral ovarian metastasis of gastric carcinoma
- 14- Sarcomas are commonly sending metastasis to L.N.s
- 15- Malignant ulcer has undermined edges & smooth floor

Q1: A female patient has a small benign pigmented lesion on the face:

What is the diagnosis?

What are the histologic type of this lesion?

What are the clinical sign, which indicate malignant transformation in this lesion?

Q2: A child has a malignant tumor of the eye globe, inoculation was done, histologic examination of the tumor shows infiltration by malignant small round cells:

What is the diagnosis?

What is the most important risk factor for this lesion?

What is the cell of origin of this lesion?

Enumerate other four sites of this lesion originating from the same cell of origin?

MCQ

Q1: Choristoma is:

- a) Benign tumor
- b) Locally malignant
- c) Tumor like
- d) Highly malignant
- e) Carcinoma in situ

Q2: The commonest site of signet ring carcinoma is:

- a) Stomach
- b) Breast
- c) Liver
- d) Lung
- e) Urinary bladder

Q3: A benign tumor in the uterine myometrium is:

- a) Rhabdomyoma
- b) Chondroma
- c) Fibroma
- d) Leiomyoma
- e) Lipoma

Q4: A biopsy from the cervix (cervical biopsy) showing dysplastic squamous epithelial cell occupying the entire thickness of epithelium with no evidence epithelial maturation and intact basement membrane is called as:

- a) Atypical hyperplasia
- b) Mild to moderate dysplasia
- c) Moderate to severe dysplasia
- d) Carcinoma in situ

Q5: A 50-year-old female present with a breast lump. Excisional biopsy was done and revealed malignant cells arranged in masses, clusters, cords with occasional glandular differentiation. These malignant cells were surrounded by dense collagenous stroma. Which of the following terms best describes the surrounding stroma?

- a) Anaplasia
- b) Desmoplasia
- c) Well differentiation
- d) Dedifferentiation

Q6: The term desmoplasia refers to:

- a) An irregular accumulation of blood vessels
- b) Maturation of spatial arrangement of cells
- c) Metastatic involvement of surrounding tissue
- d) Normal tissue misplaced within another organ
- e) Proliferation of non-neoplastic fibrous tissue

Q7: which of the following describes the histologic features choristoma?

- a) Benign neoplasm of glandular epithelium
- b) Ectopic island of normal tissue
- c) Benign neoplasm formed of benign tissue of all 3 germ like
- d) Disorganised normal tissue that form a localized mass
- e) Aggregate of epitheloid cells and chronic inflammatory cells

Q8: A 20-year-old female has an ovarian mass removed. The mass is 10 cm in diameter and cystic on cut section. The cavity was filled with hair and sebaceous like material. Histologic examination revealed a cyst wall lined by stratified squamous epithelium and show cartilage, fat, respiratory epithelium and salivary gland tissue. What is the diagnosis of such tumor?

- a) Teratoma
- b) Chondroma
- c) Hamartoma
- d) Choristoma
- e) Blastoma

Q9: Locally aggressive tumours are:

- a) Malignant tumours that invade locally & very rarely can metastasize
- b) Malignant tumours that are small in size & spread only to very near lymph nodes
- c) Benign tumours showing some cytological criteria of malignancy but not all of them
- d) Mixed tumours with both epithelial & mesenchymal cell of origin

Q10: benign tumours that can turn malignant:

- a) Melanoma & hepatoma
- b) Haemangioma & leiomyoma
- c) Colonic adenoma & neurofibroma
- d) Liver haemangioma & liver cell adenoma
- e) Seminoma & lymphoma

Q11: A 67-year-old female was diagnosed as having papillary serous cystadenocarcinoma of the ovary. She was dead and autopsy revealed multiple scattered tiny masses on the peritoneal surface with presence of marked ascites. Which of the following routes of metastases accounts for the autopsy findings?

- a) Direct extension of the tumour
- b) Haematogenous spread
- c) Lymphatic spread
- d) Transcoelomic spread

Q12: An 80-year-old male had been diagnosed as having prostatic adenocarcinoma. Histologic grading of the patient's carcinoma is based primarily on which of the following criteria?

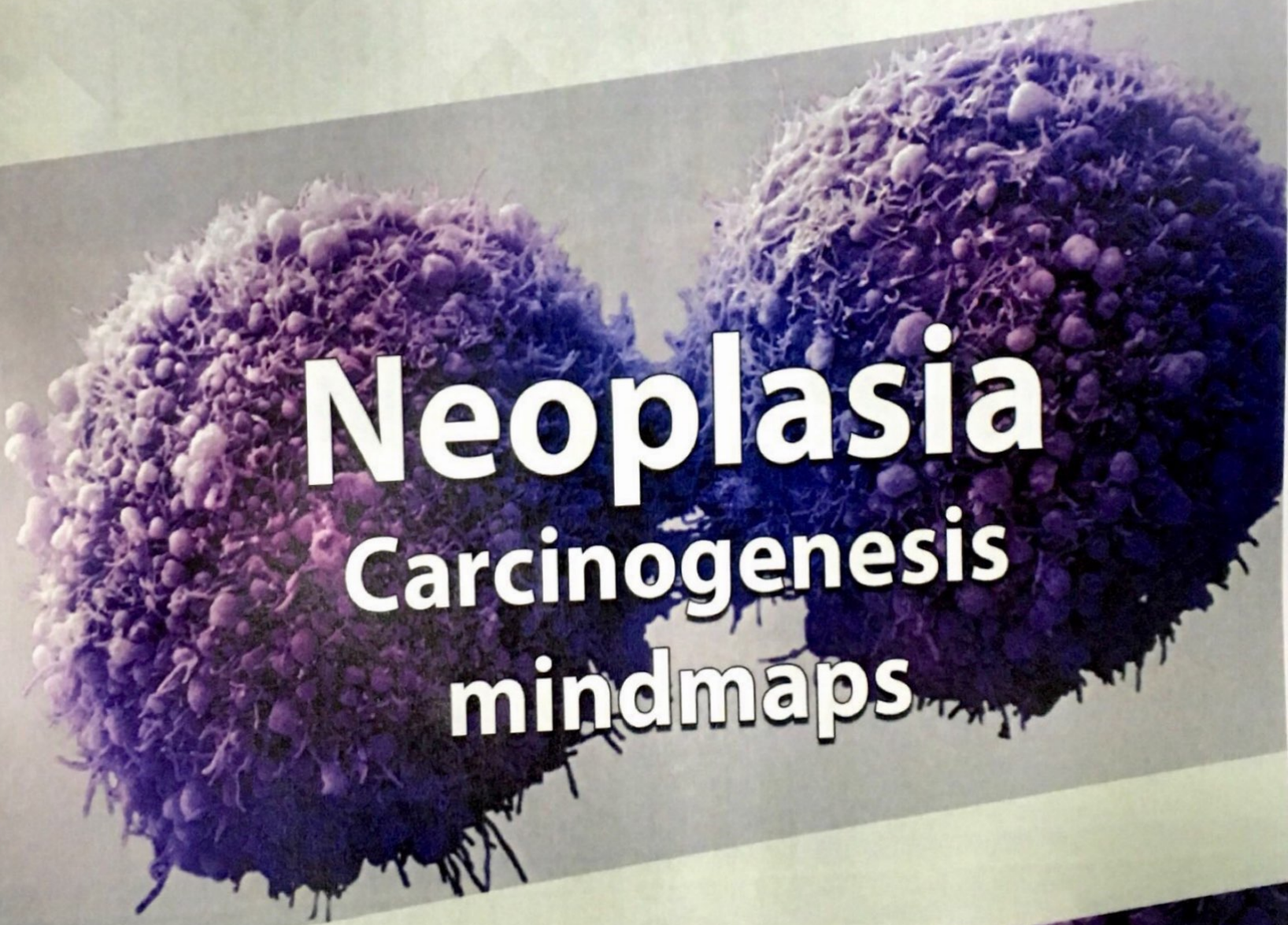
- a) Lung metastases
- b) Invasion of prostatic capsule
- c) Extent of lymph nodes involvement by malignant glands
- d) Resemblance to normal prostatic tissue
- e) Volume of prostatic gland involvement by the tumour

Q13: A 60-year-old man with hilar lung mass that was diagnosed as having squamous cell carcinoma of the main bronchus by biopsy and pathologic examination. If staging of this tumour following resection and further investigation was denoted as T1 N1 M1, which of the following findings is mostly likely present in this man?

- a) Brain metastases
- b) Infiltration of chest wall
- c) Elevation of corticotropin
- d) Poorly differentiated tumour cells
- e) Extensive lymph node infiltration

Easy Pathology

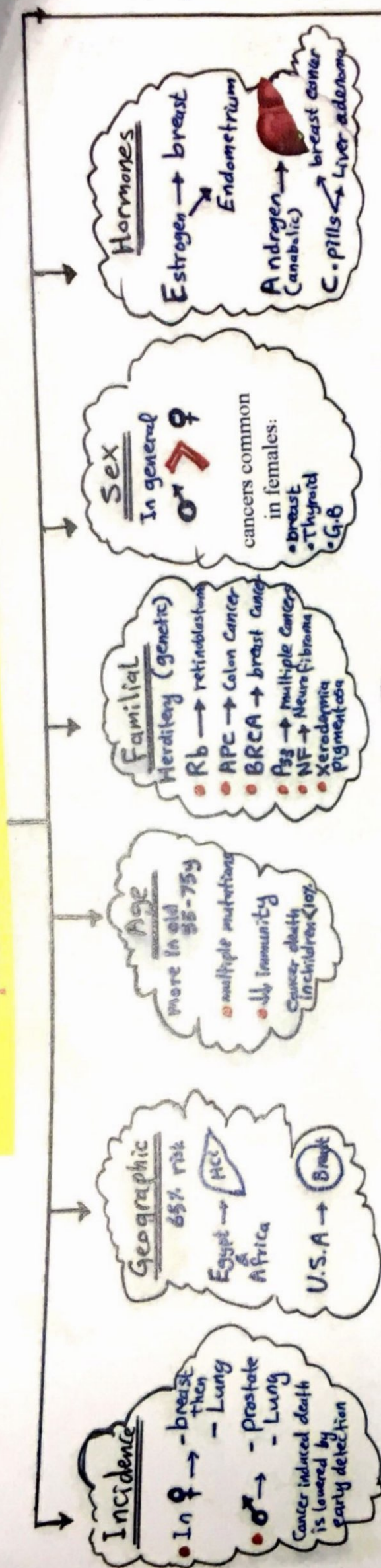
— Dr. Abdelrahman Khalifa —

A microscopic image showing two distinct clusters of cells, likely neoplastic, stained with hematoxylin and eosin (H&E). The clusters are composed of numerous small, round cells with dark nuclei and light cytoplasm, surrounded by a network of fine, fibrous connective tissue. The clusters are positioned on a light-colored background, possibly a slide or a section of tissue.

Neoplasia
Carcinogenesis
mindmaps

Ainshams 2018 - 2019

Epidemiology & P.F.



PreNeoplastic diseases (precancerous)

Y.I.P.E

edge of Marjoline ulcer
Sq.C.C.



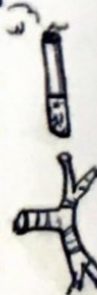
Regenerative nodules of Cirrhosis → H.C.C.



① Regenerative cells

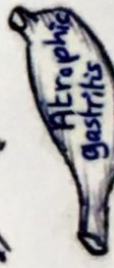
② Hyperplasia Endometrial hyperplasia ♀ → Endometr. Carcinoma

③ Dysplasia



Branchial dysplasia → Bronchogenic Carcinoma

④ Inflammations



Ulcerative Colitis → Carcinoma

⑤ Metaplasia & Leukoplakia

⑥ Benign tumors



Villus adenoma → Carcinoma

⑦ Others

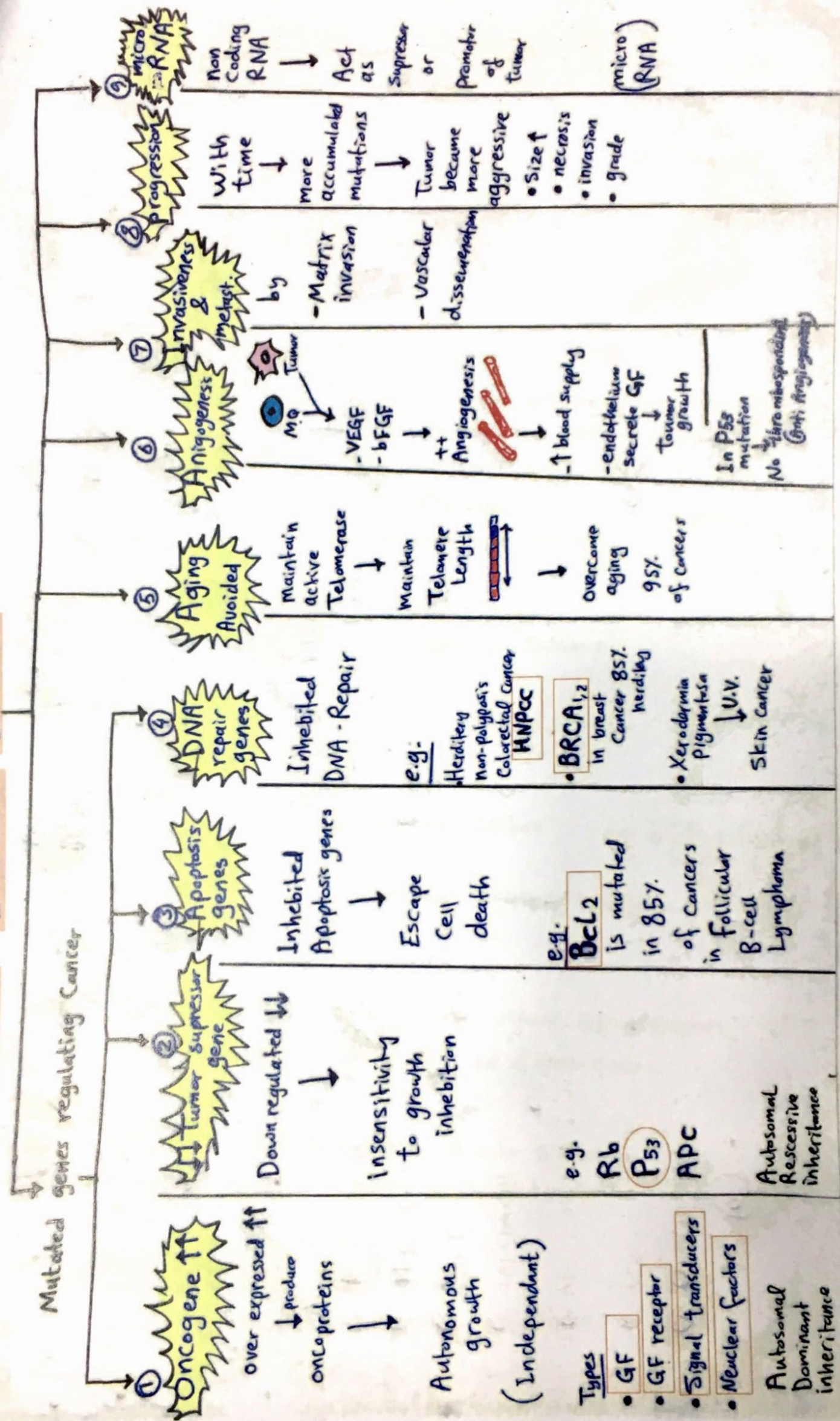


undescended testis → Germ cell tumors

neurofibroma → Sarcoma
(van Recklinghausen dis)

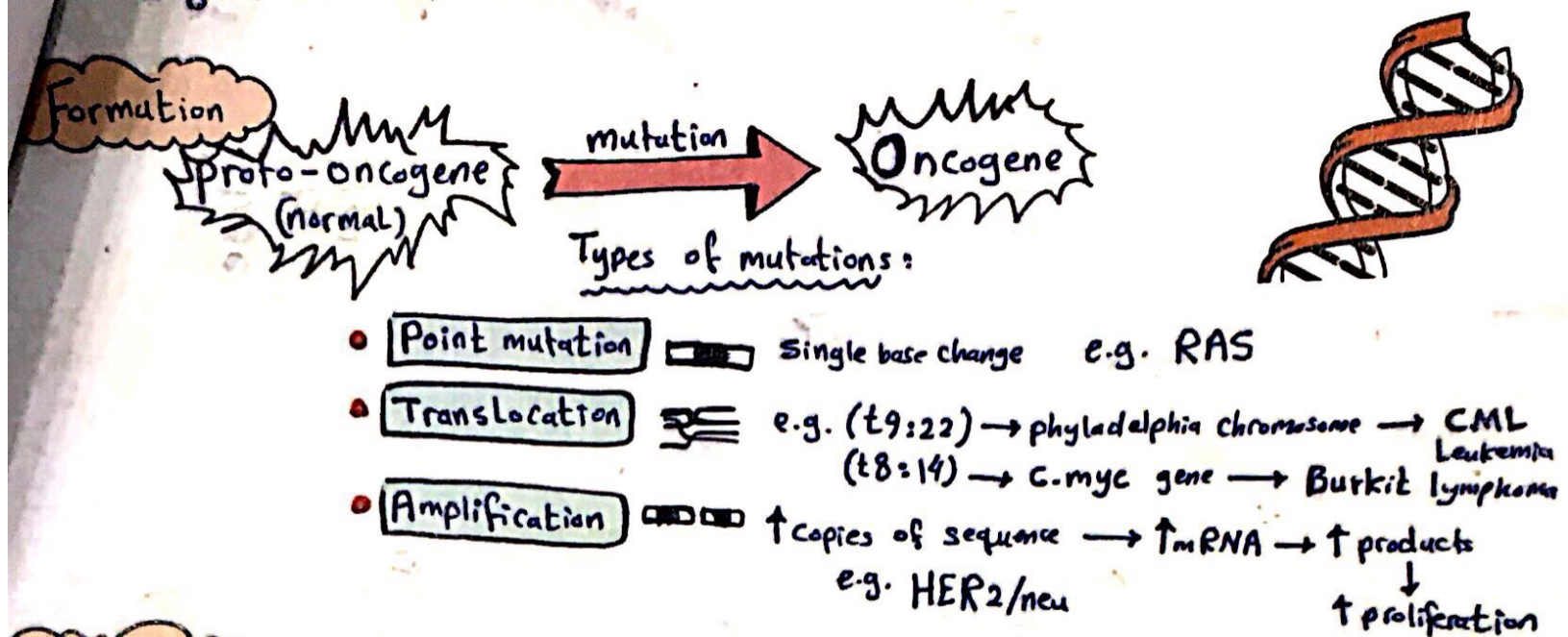
Molecular properties & Carcinogenesis

Tumor is multistep / multifactorial mutations of mono clonal cells to Acquire new properties



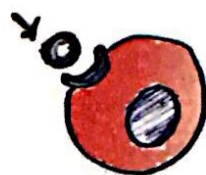
Oncogenes

A gene whose products (oncoproteins) are associated w/ tumor formation



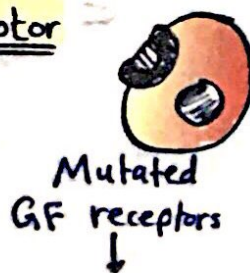
Types

① Growth Factor GF



e.g. **PDGF** in glioblastoma
TGF α in Sarcomas

② GF receptor



Direct stimulation w/out G.F.s



Over expressed receptors

Increased sensitivity to G.F.s

e.g. **EGF-r (HER2/neu)**
in 30% of Cancer breast

③ Signal transduction

e.g. **RAS**

Activate signal pathway without GF or receptors
in  30% of human cancer

④ Nuclear transcription



e.g. **MYC**

DNA transcription & enter S phase
family c-myc in Burkitt's Lymphoma

⑤ Cell cycle regulatory proteins



In normal cell **Cyclins** $\rightarrow$ $\uparrow$ **CDK** $\rightarrow$ Cell cycle progression

e.g. Some tumors produce Cyclin D e.g. Mantle Lymphoma
Cyclin dependant kinase CDK4 in Melanoma

Tumor suppressor



Tumor suppressor genes are inhibited by

* Autosomal Recessive loss of one copy
then acquired loss of the other copy

* Sporadic cases : loss of both copies is acquired

Rb

Control G₁ to S check point

If inhibited (e.g. HPV) → bypass check point

P53

In 70% of tumors → mutated

In normal cell monitors stress (e.g. hypoxia) → Activate DNA repair gene

Cell death
يقتلون أنفسهم

activates
apoptosis gene

In Case of failure



e.g. P53 mutation by DNA virus proteins

HPV
HBV
EBV

APC

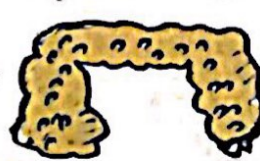
In 70% of sporadic Cancer Colon

* Normal APC → inhibits β Catenin

* In tumor APC inhibited or Lost → Active β Catenin (nuclear factor)

Cancer Colon

Adenomatous Polyps Coli
(hundreds of polyps)



Multistep Carcinogenesis

APC mutation

Hyperplasia of colon &
Hundreds of Polyps (Adenoma)

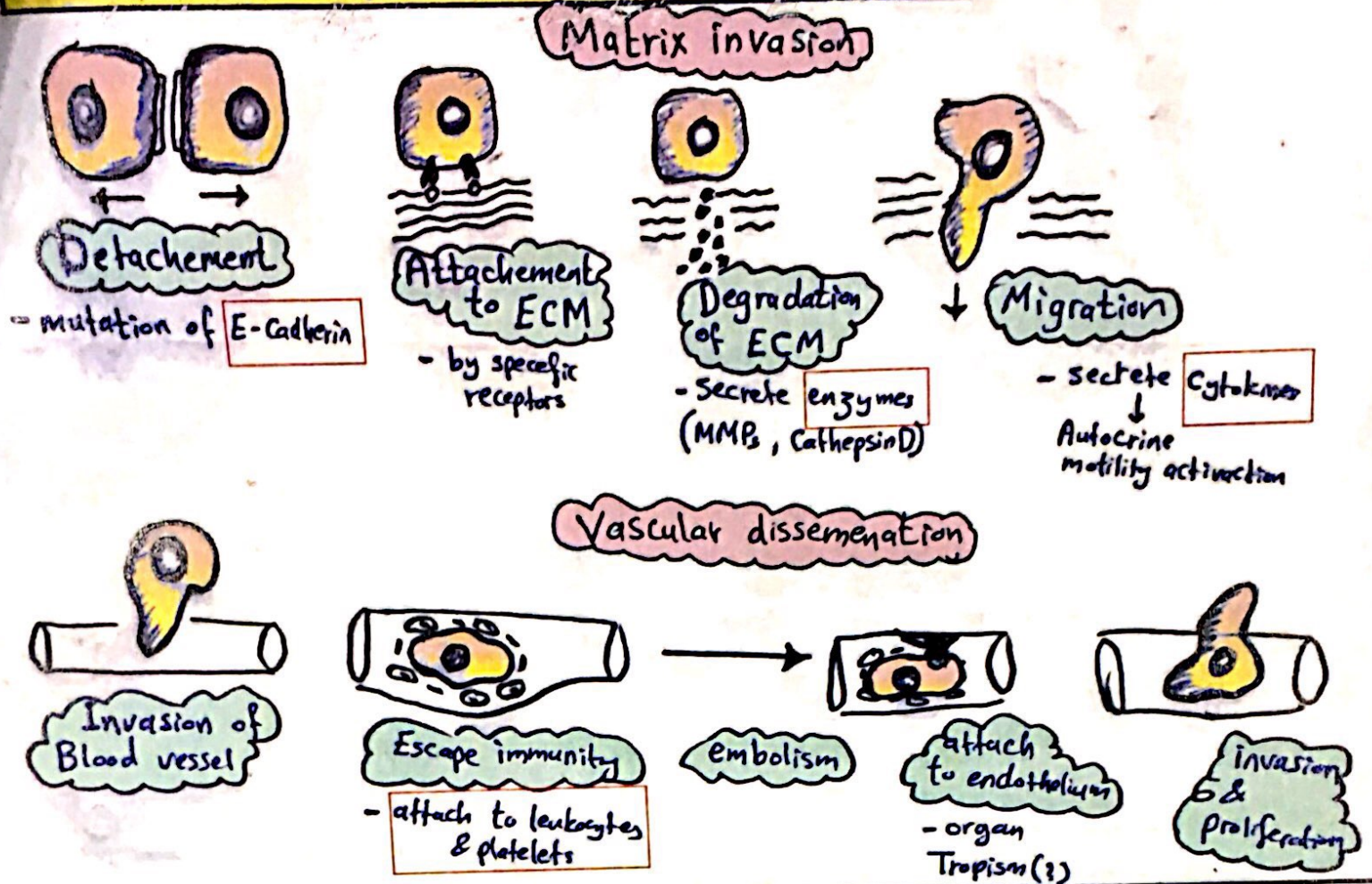
Carcinoma

K-RAS mutation

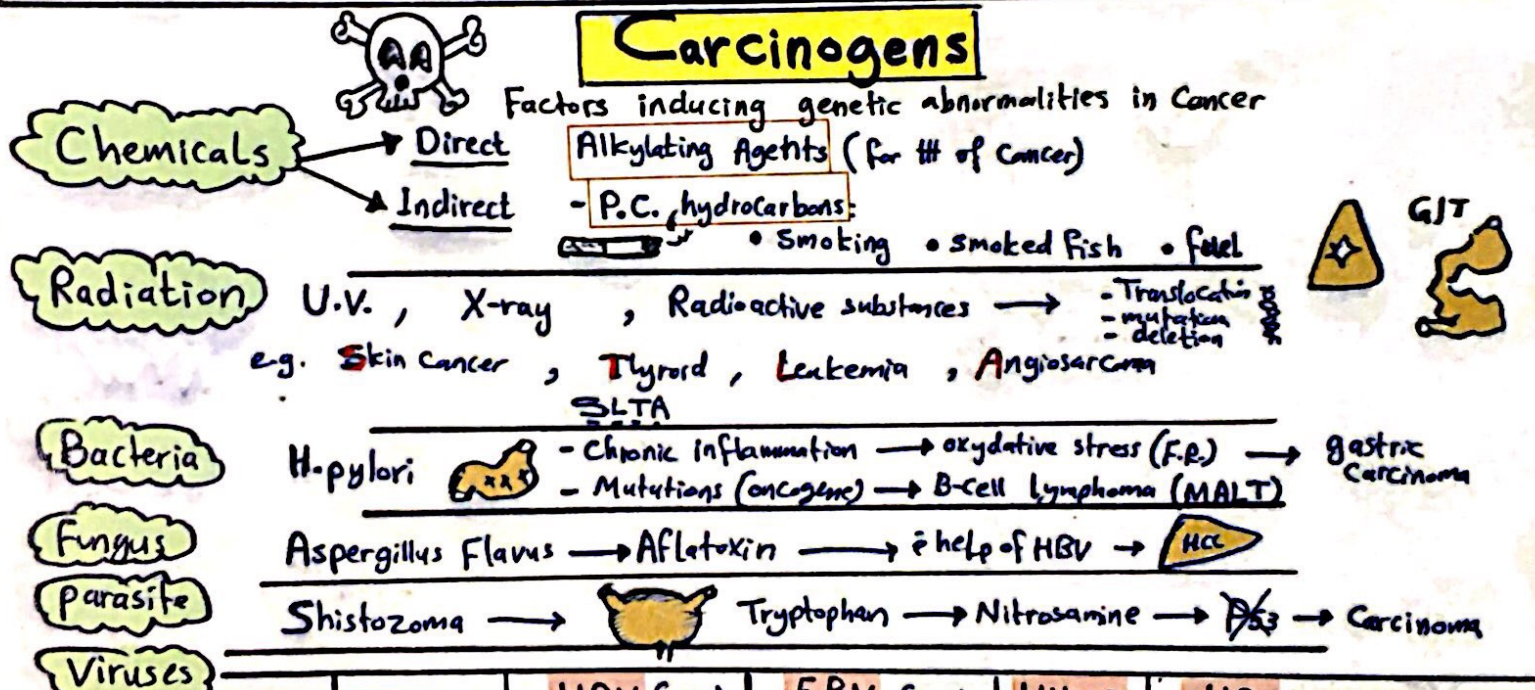
Advanced adenoma

P53 mutation

Mechanism of invasion & metastasis

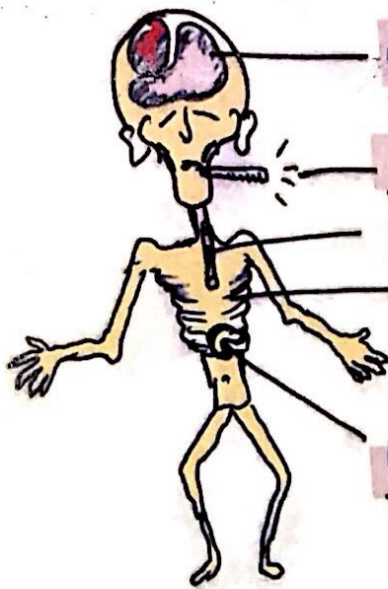


Carcinogens



HTLV-1 (RNA)	HCV (RNA)	HPV (DNA)	EBV (DNA)	HHV8	HBV (DNA)
- sexual trans. - milk ↓ IX. CDK ↑ & P53 ↓ ↓ Leukemia after 20y	Similar to HBV ↓ HCC	Type 16, 18, 31 ↓ P53 → Bax ↓ apoptosis CDK & cyclin ↓ Aging ↓ Carcinoma of Cervix, vagina, anal	↑ MYC ↓ apoptosis ↓ B lymphoma Burkitt lymphoma Hodgkin lymphoma Nasopharyngeal carcinoma	↓ AIDS Kaposi Sarcoma	- chronic inflammation F.R. - HBx protein (oncogene) signal transduction - ↓ Tumor sup. genes ↓ H.C.C.

Clinical effects



Compression

e.g. pituitary adenoma → Compress gland → ↓ function
Leiomyoma → Mucosal obstruction

Fever

cytokine - infection - ulcer - metastases
e.g. H. Lymphoma

Obstruction

of tubular organs

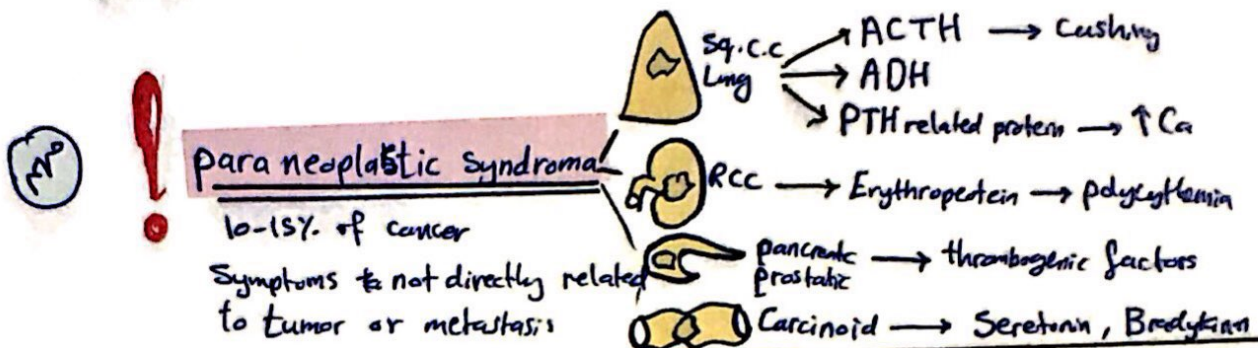
Cachexia

loss of weight + weakness + Anemia

- ↑ metabolism
- TNF & IL1 → ↓ appetite, ↓ fatty acids
- muscle damaging factor

Hormonal secretion

e.g. adenoma or adenocarcinoma



Lab diagnosis of Cancer

* Excision biopsy

Surgical Adequate Specimen



* Frozen section

Rapid technique



* FNAC

Fine needle aspiration

From palpable tumors

& Cytology



- Fast
- used in Cervix dysplasia

* Immunohistochemistry (IHC)

Tumor products

- diagnostic
- prognostic

Cytokeratin in Carcinoma

Vimentin in Sarcoma

LCA in Lymphoma

PSA in prostate

Er & Pr in breast

HER2/neu breast

* Flow cytometry

Detect Ag for phenotyping (Lymphoma)

* Tumor markers

detected in blood or tissue

PSA, CEA in colorectal & pancreatic ca
* AFP in HCC & Yolk sac tumor

* Molecular (DNA)

For hereditary cancer & diagnosis

Paraneoplastic syndromes associating cancers

Clinical syndrome	Cancer	Causal mechanism
Endocrinopathies Cushing's syndrome	Small cell carcinoma of lung, Pancreatic carcinoma	ACTH or ACTH like substance
Syndrome of inappropriate ADH secretion	Small cell carcinoma of the lung	ADH
Hypercalcemia	Squamous cell carcinoma of lung, breast & renal carcinoma	Parathyroid hormone related protein (PTHrP)
Carcinoid syndrome	Bronchial carcinoid Pancreatic carcinoma Gastric carcinoma	Serotonin, bradykinin
Polycythemia	Renal cell carcinoma	Erythropoietin
Vascular & hematologic changes - Venous thrombosis (Trousseau phenomenon) - Non-bacterial thrombotic endocarditis	-Pancreatic carcinoma -Bronchogenic carcinoma -Metastatic adenocarcinoma	Tumor products that activate clotting Hypercoagulability
Others Nephrotic syndrome	Various cancers	Tumor antigens, immune complexes

Cancer Stem cells

Some Tumors originate from stem cells which have several features:

- 1- Responsible for tumor growth and differentiation
- 2- Resistant to Chemotherapy, by expression of (MDR-1)

Angiogenesis

tumors cannot enlarge beyond 1 to 2 mm in diameter unless they are vascularized.

the 1- to 2-mm zone represents the maximal distance across which oxygen, nutrients, and waste can diffuse from blood vessels.

Neovascularization in tumor:

Angiogenesis: formation of new capillaries from existing vessels

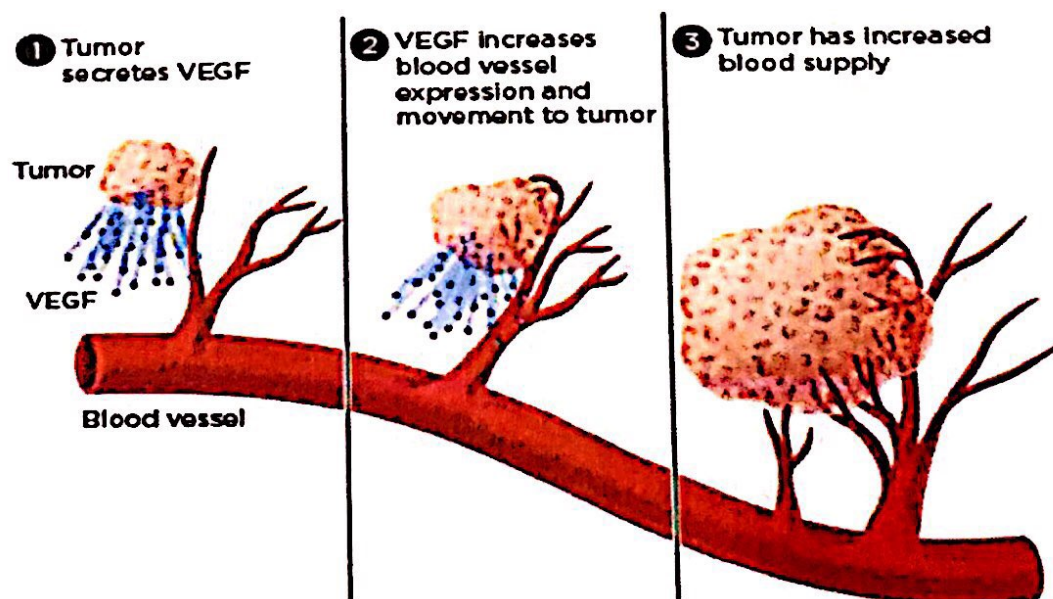
Vasculogenesis: formation of new capillaries from endothelial cell precursors

Role of neovascularization:

- 1-Perfusion supplies needed nutrients and oxygen
- 2-endothelial cells→ stimulate the growth of adjacent tumor cell

(insulin-like growth factors, PDGF, and colony-stimulating factor)

- 3-Access to the vasculature and hence for metastasis.



Dr. Abdelrahman Khalifa

Mechanism of cancer angiogenesis:

- Proteases → release the angiogenic **basic FGF** stored in the extracellular matrix (ECM)
- Thrombospondin (**TSP-1**), is produced by fibroblasts in response to signals from the tumor cells.
- **Hypoxia** in large tumors → activation of hypoxia-inducible factor- 1α (**HIF-1 α**) → stimulates production of **VEGF**

Normally, a product of gene **VHL** inhibits VEGF release. (in cancer VHL cannot inhibit VEGF)

- Angiogenesis inhibitors— (**angiostatin**, **endostatin**, and **vasculostatin**)—are produced by cleavage of tissue matrix (e.g. collagen)
But they are not enough to stop angiogenesis

Targeting VEGF by Antibodies is approved for cancer therapy

Invasion of Extracellular Matrix (ECM)

- **E-cadherin function** is lost in almost all epithelial cancers, either by mutation, or by activation of β -catenin genes, or by **SNAIL** and **TWIST** transcription factors
- local degradation of the basement membrane and interstitial connective tissue.
 - secrete proteolytic enzymes
 - induce fibroblasts and inflammatory cells to elaborate proteases.
- Fragmented products of collagen and proteoglycans also have chemotactic, angiogenic, and growth-promoting effects.
- attachment of tumor cells to ECM proteins
- Locomotion of tumor cells (by actin filaments) activated by tumor cytokines

Direction : Autocrine motility factors + some growth factors → chemotactic activity for tumor cells.

organ tropism may be related to the following mechanisms:

- Expression of adhesion molecules by tumor cells whose ligands are expressed preferentially on the endothelium of target organs
- Expression of chemokines and their receptors.

Q14: Malignant epithelial cells would most likely show decreased expression of which of the following?

- a) Tumour necrosis factor
- b) E_cadherin
- c) Vascular endothelial growth factor
- d) Telomerase

Q15: Which of the following changes in cell behavior is the first step in the process of metastases?

- a) Stimulation of angiogenesis
- b) Circulating in blood or lymph vessels
- c) Exit from circulation into a new tissue
- d) Penetration of vascular or lymphatic vessels
- e) Invasion of underlying basement membrane

Q16: A 55-year-old female had an 8 cm left breast mass diagnosed as high-grade invasive duct carcinoma. A chest CT scan revealed bilateral lung canon ball nodules. The presence of pulmonary nodules is most likely related to which of the following?

- a) Proximity of breast carcinoma to lungs
- b) Extensive lymphatic connection between breast and pleura
- c) Expression of estrogen receptors in nuclei of breast carcinoma cells
- d) Vascular pulmonary ligands that bind to adhesion molecules on carcinoma cells

Q17: Which of the following carcinogenic agents is the most important in skin cancer?

- a) Aflatoxin
- b) Vinyl chloride
- c) Sunlight
- d) Asbestos

Q18: Endometrial adenocarcinoma can be preceded by which of the following changes in endometrial tissue?

- a) Atrophy
- b) Hypertrophy
- c) Metaplasia
- d) Hyperplasia

Q19: The neoplastic cells most likely acquire a set of mutation that cause, which of the following changes in cell behavior?

- a) Decreased cellular motility
- b) Increased cell-cell adhesion
- c) Increased susceptibility to apoptosis
- d) Loss of cell cycle check point control

Q20: Compare to a normal adult somatic cells, cancer cells would most likely show high level of expression of which of the following proteins?

- a) Desmin
- b) Dystrophin
- c) Cytochrome c
- d) P selectin
- e) Telomerase

Q21: A 65-year-old female had undergone total abdominal hysterectomy for uterine leiomyosarcoma. One year later a chest x-ray revealed a 4 cm nodule in her right lung. Ultra sound guided biopsy and histopathologic examination revealed a poorly differentiated sarcoma. The patient's medical history indicate that she had smoked cigarettes most of her adult life.

Which of the following mechanisms best explain these findings?

- a) Continued cigarettes smoking by the patient
- b) Development of a second primary neoplasm
- c) Inheritance of a defective RB gene
- d) Metastases from an aggressive tumour sub-clone

Q22: A 55-year-old female complained of breast mass that surgically excised by modified radical mastectomy with axillary clearance and was diagnosed as invasive duct carcinoma T3 N1 M1. She had no family history of breast cancer. Which of the following molecular abnormality is most likely to be found in the carcinoma cells?

- a) Amplification of EGFR2 (Her2) gene
- b) Inactivation of one BRCA 1 gene copy
- c) Deletion of one RB gene copy
- d) Mutation of one p35 gene copy
- e) Fusion of BCR and ABL genes

Q23: A 25-year-old female was diagnosed as having an invasive duct carcinoma. The patient's older sister was recently diagnosed with ovarian cancer and 3 years ago her maternal aunt had performed mastectomy for a diagnosis of invasive duct carcinoma. Which of the following mutated genes would most likely be present in this family?

- a) BRCA 1
- b) EGFR 1
- c) RB
- d) BCL2
- e) RAS

Q24: A 58-year-old heavy smoker man presents to the emergency department with shortness of breath and haemoptysis. Chest x-ray demonstrates a large left central lung mass. The serum calcium is 13 mg/dl (normal 8.5 to 10.2). The metabolic abnormality described here is likely due to elaboration of which substance?

- a) Erythropoietin
- b) Antidiuretic hormone
- c) Carcinoembryonic antigen
- d) Parathyroid-related hormone
- e) Adrenocorticotrophic hormone-like substance

Q25: A 68-year-old man has a long history of prostate cancer that was metastatic at the time of diagnosis. Over the past 2 months, he has had significant weight loss, loss of appetite, and loss of energy. His current spectrum of conditions can be attributed to which of the following?

- a) Interleukin-2
- b) Fibroblast growth factor
- c) Tumor necrosis factor alpha
- d) Platelet-derived growth factor
- e) Vascular endothelial growth factor

Q26: Which of the following neoplasm is most likely to arise following viral infection?

- a) Retinoblastoma
- b) Small cell carcinoma of the lung
- c) Prostatic adenocarcinoma
- d) Hepatic angiosarcoma
- e) T cell leukemia

Q27: Which of the following is considered a risk factor for papillary thyroid carcinoma?

- a) Repeated viral infection
- b) Exposure to radiation
- c) Blunt trauma from a fall
- d) Exposure to arsenic compounds

Q28: Epstein Barr virus infection can increase the risk of which of the following neoplasms?

- a) Kaposi sarcoma
- b) Small cell carcinoma of the lung
- c) Osteosarcoma
- d) Nasopharyngeal carcinoma
- e) Endometrial carcinoma

Easy Pathology

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Granuloma



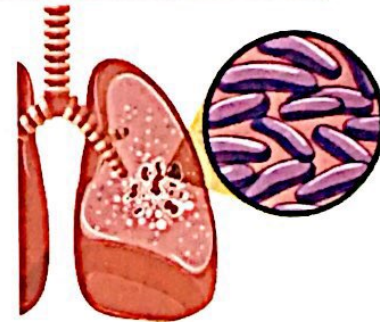
Ain Shams 2018 -2019

Granuloma

Chronic non specific inflammation, forming mass of Epithelioid cells, surrounded by lymphocytes

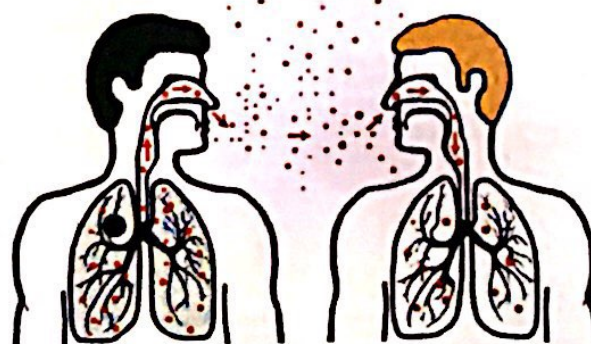
- **Infective**
 - Bacterial: **TB**, Cat scratch disease
 - Parasitic: **Bilharziasis**, Filariasis, Toxoplasma
 - Fungal: **Mycetoma**, Blastomycosis, Cryptococcus
- **Foreign body** granuloma : Silica, Suture, and Silicon granuloma in breast
- **Idiopathic** : **Sarcoidosis**, Crohns disease

Tuberculosis



Aetiology

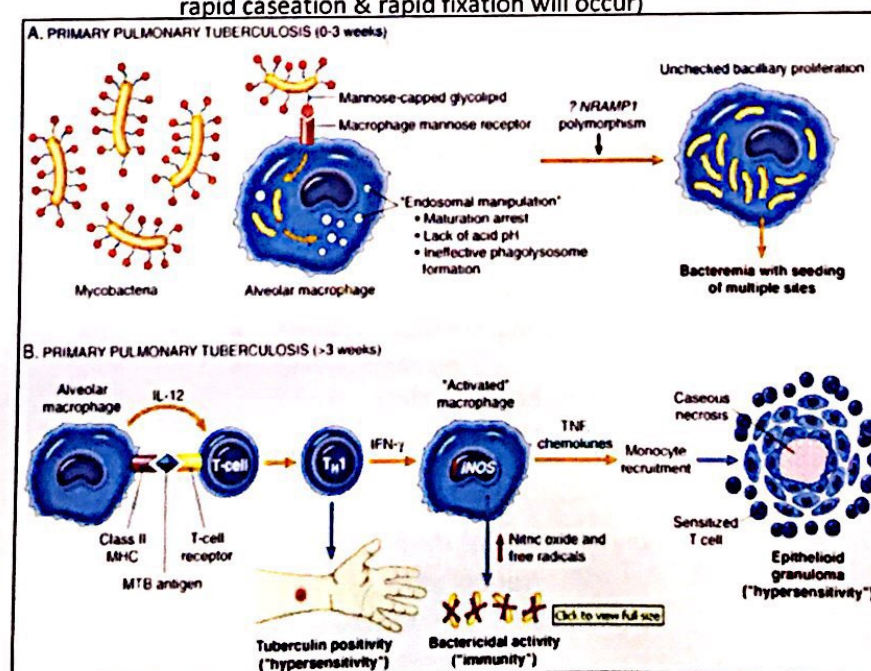
- **Organism:** **Mycobacterium TB** (*Human type* - *Bovine type*)
 - **Structure:** Cylindrical , contain **Antigenic Protein**, **Carbohydrate**, and **Lipid Capsule** (Resist heat , dryness, Lysosomes, F.R., Acid fast, alcohol fast)
 - **Virulence:** *Non motile, non toxin producing, killed by U.V.*
 - **Stain** (*stained with Ziehl-Neelsen*)
- **P.F. :**
 - **Low immunity** (*AIDS, D.M., Malnutrition, Alcoholism, Silicosis*)
 - **Crowding** (inhalation)
 - **Genetic** (Afro-American) : mutated **NRAMP1** (natural resistance associated macrophage protein 1) → decreased killing ability of macrophage
- **Mode of transmission**
 - **Inhalation** : *droplets – dust* → **Tonsils - Lung**
 - **Ingestion** : *raw milk, or infected sputum* → **tonsils - intestine**
 - **Inoculation:** *Infected meat – Infected materials* → **Infect Skin wounds (rare)**
 - **Intrauterine:** *transplacental* → **congenital TB**



Pathogenesis & Host response to T.B.

• Proliferative reaction (cellular reaction)

- Neutrophils are attracted → **destroyed** by organisms
- Lipid part of bacteria → attract **Macrophage** → phagocytosis of bacteria → replicate inside macrophage → without lysosomal damage
- Macrophage → secrete IL-12 & present Ag to **T Lymphocytes** after **3 weeks**
Th0 → became **T helper1 CD4**
- **Th1 CD4** → (hypersensitivity type IV) → secrete several Lymphokines:
 - **IL2** → proliferation of lymphocytes
 - **IFN-gamma** → Activation of macrophage(strong killers & contain NO free radical)
 - Activated macrophage → secrete **TNF** → aggregation & transformation into → **Epithelioid cells**
 - Activated macrophage → **PDGF, TGF-B** → enhance fibrosis
 - Epithelioid cells :large, with abundant cytoplasm, vesicular nucleus, indistinct membrane
 - Epithelioid cells became → Giant cells:
 - **Langhan's giant cell**: Multineucleated, horse-shoe arrangement
 - **Foreign body giant cell**: clustered nuclei in the center or one pole
 - **MIF** → Fixation of epithelioid cells & giant cells
 - Activation of **CD8** → **Casation** cytotoxic factor → Kill macrophage → Tissue caseation
 - **Inflammatory mediators** → +ve skin test
 - **Transfer factor** → immune system sensitization (In case of 2ry T.B. → rapid caseation & rapid fixation will occur)



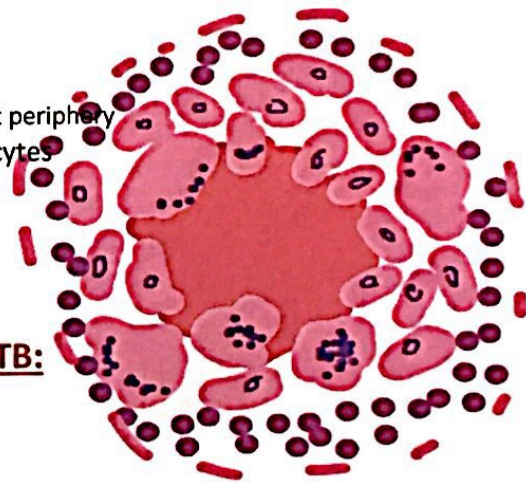
- **Exudative reaction (excess fluid exudate)**
 - Occur in Serous sacs
 - In More Sensitive individuals (excess T lymphocytes)
 - More Severe infection due to less immunity

Gross: tubercles, grey then → yellowish white (caseation) , Firm → soft cheesy



Microscopic: Tubercle (granuloma)

- **Early:**
 - Epithelioid cells (describe?)
 - Giant cells (describe?)
 - Lymphocytes (peripheral)
- **Late**
 - Caseation: homogenous pink, contain bacteria at periphery
 - remnants of cells : Epithelioid, giant, lymphocytes
 - Fibroblasts surrounding granuloma



Fate and complication of TB:

- Fibrosis
- Capsulation → Reactivation
- Calcification
- Cold abscess (extensive liquefaction of caseation) in Bone, joints, LN, testis
 - It accumulates or open by a tract of granulation tissue (sinus)
- Severe Caseation → bleeding, & blood spread
- Secondary Amyloidosis (discussed later)
- Spread:
 - **Local** : by macrophage (bacteria is non-motile)
 - **Lymphatic** (More In 1ry TB) → TB Lymphangitis & TB Lymphadenitis.
 - **Blood** (More in 2ry TB)
 - Caseation → penetrate blood vessels arteries or veins
 - Arterial invasion → spread in same organ
 - Venous invasion → spread into different organs
 - Spread could be:
 - Limited spread (in single organ) → isolated organ TB
 - Disseminated (less immunity) → Miliary TB in multiple organs
 - **Natural passages :**
 - Bronchi, from tonsils or larynx
 - Bladder, from kidney
 - Peritoneum from TB salpingitis
 - Pleural spread

	1ry TB	2ry TB
Infection	1 st time infection No sensitization	2 nd time infection (Reactivation – Reinfection) Sensitization present → exaggerated response
Age	More in Children	More in Adults
Sites	Tonsils – Lung – Intestine – Skin	Previous organs or Any site
Caseation	Less	More extensive
Pathological lesion	1ry complex: TB focus Lymphangitis Lymphadenitis (e.g. Tabes mesenterica)	L.N. & lymph vessels are <u>less</u> affected
Blood spread	Less	More

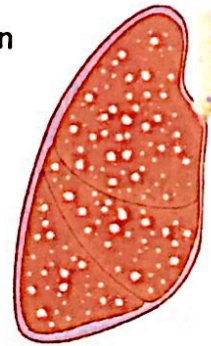
Miliary T.B. Multiple tuberculous foci due to blood spread in the same organ or distant organs

Causes: blood spread

Gross: multiple foci – small 2mm – grayish white – rare caseation

micro: granuloma (no fibrosis- no caseation)

Fate: Systemic miliary TB in multiple organs → fatal



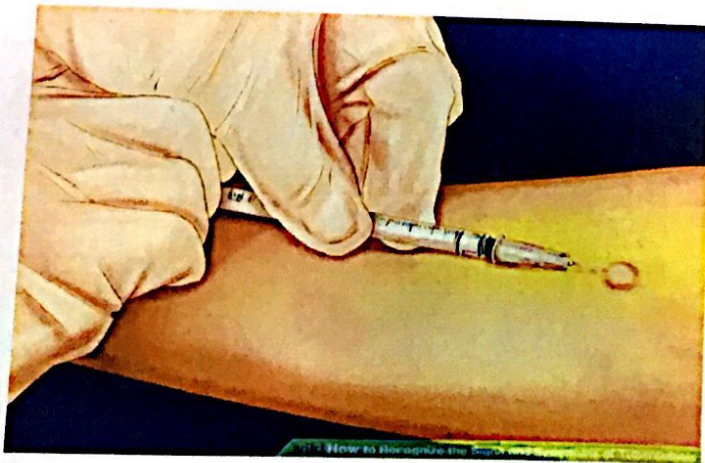
N.B.

Immunization

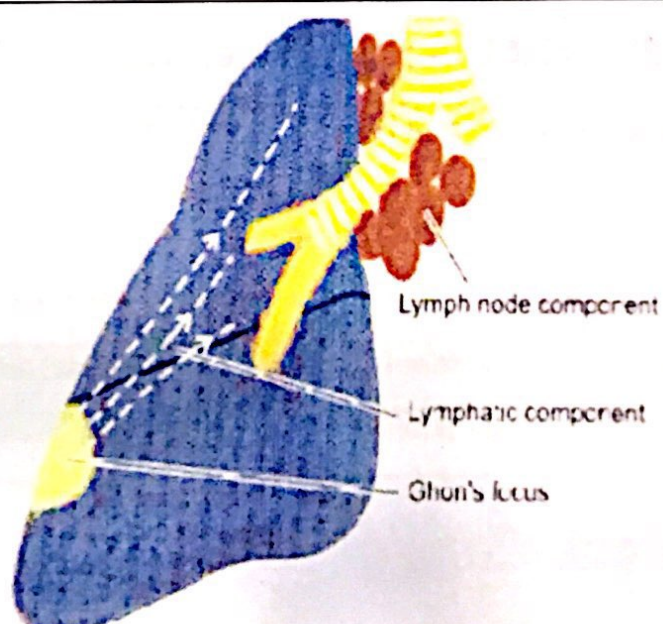
BCG (Attenuated bovine bacteria), given by injection → induction of hypersensitivity (cell-mediated) → Skin lesion is healed by fibrosis

Tuberculin test

Injection of 0.1 ml of (PPD) → Skin induration 0.5 cm within 2 days → patient is infected or immunized

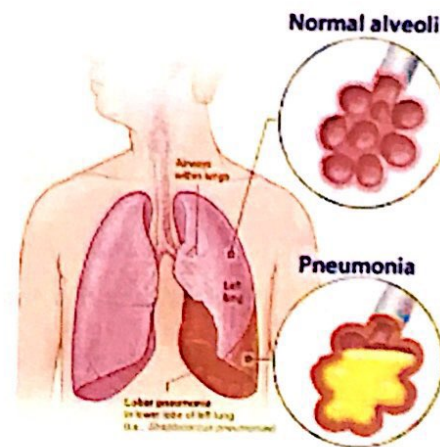
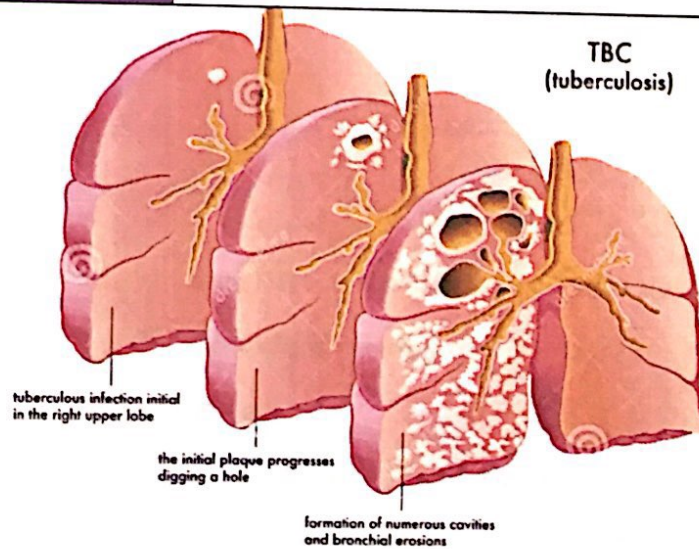


	1ry pulmonary TB Childhood TB	2ry pulmonary TB Adulthood TB
Infection	1 st time infection (inhalation)	Re infection in sensitized patient Reactivation (in AIDS, Cancers, Cortisone)
Age	More in Children	More in Adults
Sites	-Right lung -Between upper & lower lobes -Peripheral (sub-pleural)	Re infection : Apex (less blood, more air, more lymphatics) Re activation : previous site of Gohns focus
Morphology	1ry pulmonary complex: 1- Ghon's focus 1-2 cm (yellowish white- soft cheesy – rounded) <u>micro</u> : ...describe.... 2- Lymphangitis (Chain of tubercles) 3- Lymphadenitis (hilar LN)	- Assman's focus Apical TB focus 1-2 cm (describe..)→ cavitation & fibrosis <u>Pathogenesis</u> : Preexisting sensitization → Less L.N. enlargement , but more caseation
Fate	- <u>Fibrosis & calcification</u> -Capsulation & reactivation <u>-In Low immunity :</u> <i>Progressive TB: Acute TB pneumonia</i> <i>Spread: Lymphatic & blood (military)</i>	-Regression by fibrosis (<i>good immunity</i>) -Progression (<i>low immunity</i>): 1-Progressive Chronic fibro-caseous TB 2-Acute TB pneumonia

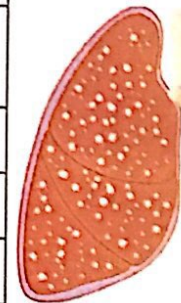


Progressive pulmonary TB

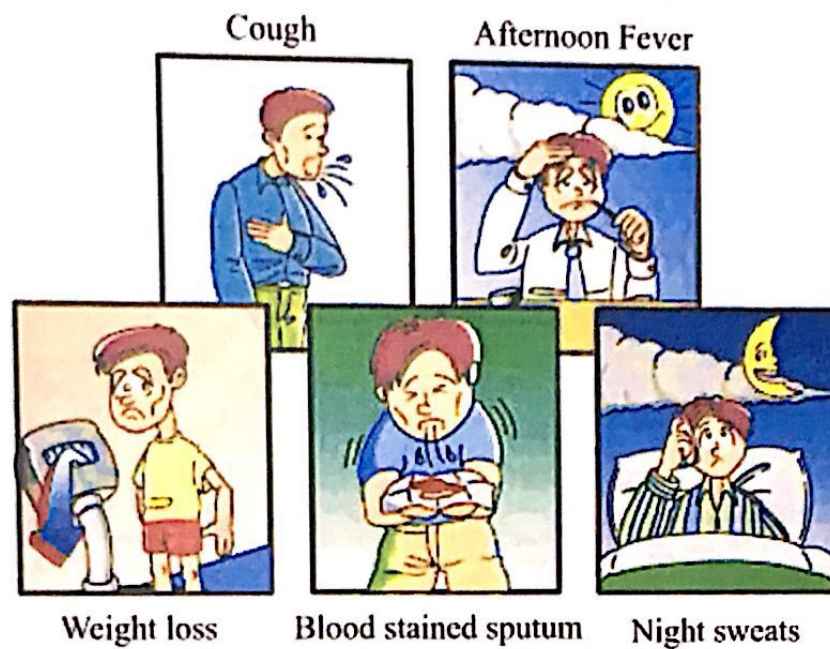
	Chronic fibro-caseous TB	Acute TB pneumonia
Course	Chronic, slowly progressive	Rapidly fatal TB
Immunity	Better Immunity Less Hypersensitivity	Immunity is very low (e.g. AIDS) more Hypersensitivity
Morphology	- Apical Cavity is irregular surrounded by fibrous capsule. Cavity is traversed by perforated bronchi & blood vessels. - Multiple small basal foci - L.N.: Minimal enlargement	- Consolidation in middle and lower lobe - No cavitation - L.N.: Enlargement (rapid spread)



Chronic fibro-cas. TB	Miliary TB
Spread through bronchi or lymphatics	Spread through blood vessel
less numerous	More numerous lesions
Larger & variable in size	Small foci (1-2 mm)
Yellowish (caseation)	Grayish white (no caseation)
Minimal L.N. enlargement	No L.N. enlargement



Clinical picture of Pulmonary TB



complications of pulmonary TB

- Lung Fibrosis & calcification → right sided H.F.
- Cavitations : perforate → hemoptysis ruptured → pneumothorax , TB Empyema
- Spread:
 - Local → bronchitis, pleurisy , pericarditis
 - Lymphatic → T.B. Lymphadenitis → bronchial compression & dyspnea
 - Blood → Miliary TB
 - Sputum → 2ry TB of tongue, tonsils, larynx & 2ry intestinal TB
- Secondary Amyloidosis → Nephrotic syndrome

Sites of Primery complex

- 1ry cervical complex : TB focus in tonsils + Lymphangitis + Cervical Lymphadenitis
- 1ry pulmonary complex: Ghon's focus + Lymphangitis + Hilar Lymphadenitis
- 1ry intestinal complex: TB focus in small intestine + Lymphangitis + mesentric Lymphadenitis (tabes mesentrica)

2ry intestinal TB

- swallowing sputum from Lung
- Reactivation or re-infection (bovine)

More in Adults

Ileum → cecum → ascending colon

- 1- Multiple fused ulcers → girdle ulcer
Undermined edge, caseating floor, transverse ulcers
- 2- Minimal LN enlargement



Complications of TB +

-Complications of Ulcer:

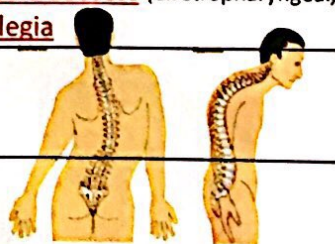
Bleeding – 2ry infection – fibrosis and stenosis – perforation and fistula

TB of L.N.

- **Common Sites:** Cervical LN – Hilar LN – Mesenteric LN (why?)
- **Gross:** Enlarge, firm, discrete then → Fused (matted) and cheesy
- **Complications:** complications of TB (*enumerate...?*) + Cold abscess → sinus

TB of vertebrae (pott's dis)

- **Gross:**
 - Tubercles (*describe*) at the lower thoracic, upper lumbar vert. → caseation
 - Caseation of vertebral bodies with damaged intervertebral disc
- **Complications:** complications of TB (*enumerate...?*) + Cold abscess (e. retropharyngeal, mediastinal, lumbar) + Deformities (kyphosis, scoliosis) + Paraplegia



Schistosomiasis

Aetiology:

- **Organism:**
 - *Schistosoma hematobium* (urinary, genital)
 - *Schistosoma Mansoni* (intestinal, hepatic)
- **Mode of transmission** : penetration of skin under water

Pathogenesis:

1- Cercaria:

- Allergic Rash (penetration of skin → *type I* hypersensitivity) red macules, or papules

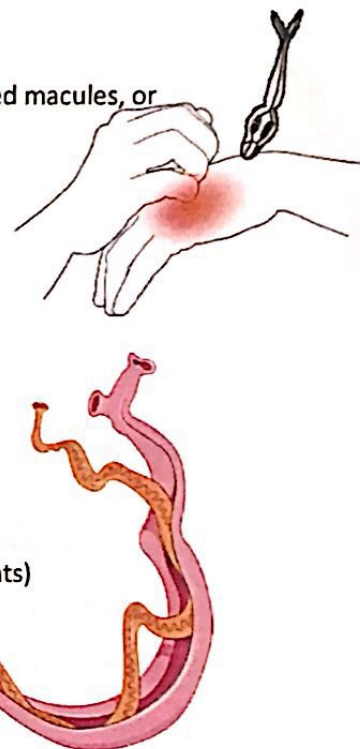
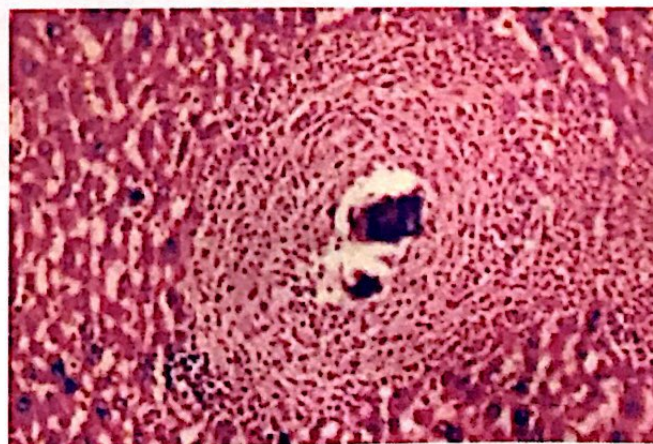
2- Worm

- Living worm
 - Not antigenic (covered by self protein)
 - Hemozoin pigment is taken by RES
- Dead worm
 - Embolism of veins by dead worm
 - Necrotizing-phelebitis
 - Angiomatoides , new capillaries (small arterio-venous shunts)

3- Ova:

- Granuloma :
 - Cellular granuloma: macrophage – Epithelioid cells – giant cells – **eosinophils**
 - surrounded with fibroblasts
 - healing with fibrosis

(Ova contain meracidium. Ova could be living, dead or calcified)

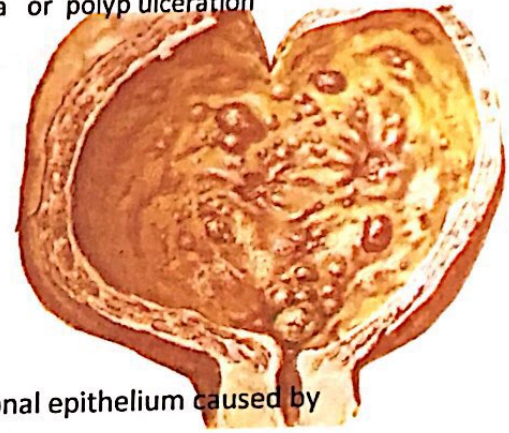


Urinary bilharziasis

Site: Trigone and posterior wall (ureteric orifices) – submucosa is the common site (?)

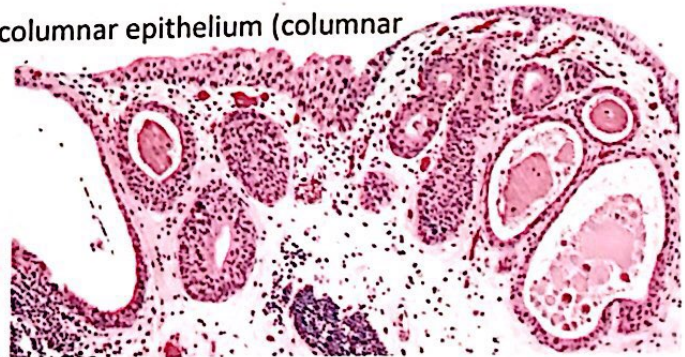
Gross:

- **Grain-like nodules** (yellow – surrounded by congestion)
- **Sandy patches** (granular dirty yellow patches – calcified ova in the wall + mucosal atrophy)
- **Polyps** Gross: Shape: sessile, or pedunculated or mulberry - Size: 2mm-2cm - red
Micro: Core: granulation tissue + granuloma (describe) - Covering: hyperplasia
- **Ulcers** : small - may fuse together (healing is difficult due to ova and fibrosis)
caused by: sandy patches or penetration by ova or polyp ulceration
- **Mucosal vesicles** (cystitis cystic)
- **Fibrosis of the wall or orifices**



Microscopic:

- Bilharzial granuloma + bilharzial ova
- Epithelial (Urothelial) changes:
 - **Hyperplasia & brunn's nest:** mass of transitional epithelium caused by dipping in submucosa (no invasion)
 - **Squamous metaplasia:** transform into str. Squamous → (precancerous)
 - **Leukoplakia:** excess keratinization of str. Squamous → (precancerous)
 - **Dysplasia & CIS:** cytological changes similar to cancer → (precancerous)
 - **Cystitis cystica:** cystic changes in brunns nest → lined by transitional ep
 - **Cystitis glandularis:** cyst lined with columnar epithelium (columnar metaplasia) → (precancerous)



Complications:

- ☑ Bleeding → terminal hematuria → anemia
- ☑ 2ry infection of ulcers → pH changes → stones
- ☑ Fibrosis & contracted bladder :
 - closed bilharziasis → spread → pulmonary bilharziasis
 - Urinary tract obstruction → Urinary diverticulae - Hydronephrosis → **renal failure**
- ☑ Perforation → fistula
- ☑ Precancerous lesions (enumerate?) → **Carcinoma**

Intestinal bilharziasis

Aetiology: Schistosoma mansoni > hematobium

Site: Large intestine (Rectum) – submucosa is the common site (?)

Morphology:

- Early : swollen red mucosa with petichae
- Late: sandy patches – polyps- ulcers – fibrosis

Complications:

- ☒ Bleeding → anemia
- ☒ 2ry infection of ulcers → dysentery
- ☒ Fibrosis → closed bilharziasis → spread → hepatic bilharziasis
- ☒ Perforation → fistula - peritonitis
- ☒ Polyps → intussusceptions & intestinal obstruction



N.B : No precancerous epithelial lesions in intestinal bilharziasis

Hepatic bilharziasis

Pathogenesis: Following old intestinal bilharziasis (schistosoma mansoni) → intestinal fibrosis → **ova** accumulate in mesenteric veins → portal vein → deposits in **portal tracts** → granuloma & hepatic **periportal fibrosis**

Dead worm → emboli , thrombo-phlebitis & angiomatoid formation → portal hypertension

Gross	Size: early large → late : reduced Surface: irregular retracted (<i>not cirrhotic</i>) C/S: thick white PT Coarse portal tracts are thick (<i>pipe stem fibrosis</i>) Cons: firm	
Microscopic	-Portal tracts: ova & Granuloma (<i>describe ...</i>) Lesions by dead worm (<i>enumerate</i>) Bile duct proliferation -Parenchyma: Kupffer cell contain bilharzial pigment Pigment in kupffer cells	

Complications of Hepatic bilharziasis:

- **Portal hypertension & portal vein thrombosis**

- **causes:** Portal tract fibrosis + Angiomatoides + parasitic emboli

- **Effects:**

- Congestive Splenomegaly
 - Ascitis (due to portal hypertension & hypoalbuminemia), which is Late and indicates bad prognosis
 - Dilated porto-systemic veins



- **esophageal varices** (submucosal blue bands) → **hematemesis**

- **caput medausa**

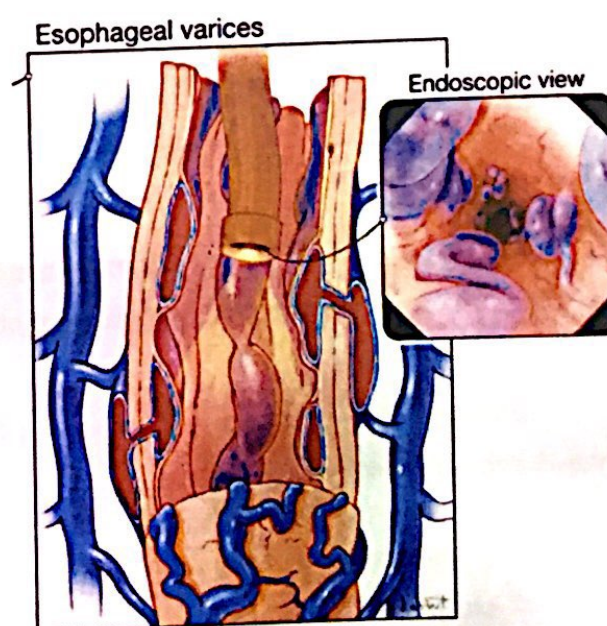
- **Piles** → **bleeding P/R**

- Other complications of porto-systemic shunts:

- **Ammonia encephalopathy:** toxic ammonia pass from intestine to brain through porto-systemic veins. And aggravated by disturbed liver function

- **Pulmonary bilharziasis:** ova pass from intestine to systemic veins

- **Minimal disturbance of liver function**



Splenic bilharziasis

Circulating Ag → hyperplasia of lymphoid tissue
 Hepatic bilharziasis → portal hypertension → congestion of spleen

Gross: Large, brown, Thick capsule with cartilaginous metaplasia

Microscopic:

- Red pulp & sinusoids: dilated congested → ruptured → hemorrhage → forming **gandy-gamna** nodules (hemosiderin + Fibrosis)
- White pulp: *Atrophic lymphoid follicles*
- Littoral cell contain hemosiderin
- Capsule & trabeculae : thick
- Ova in spleen are not common



Complications: Compression & Hypersplenism

Pulmonary bilharziasis

Aetiology:

- Schistosoma **hematobium** (spread from urinary through systemic veins or vertebral)
- Schistosoma **Mansoni** (spread from intestinal → through porto-systemic veins)
- Miracidium in ova → secrete cystine → Antigenic

Pathological changes

- Cercaria: irritation & cough
- Ova: granulomas (*describe..*) → fibrosis → pulmonary hypertension (with smooth muscle proliferation in arterioles)
- Dead worm:
 - *Necrotizing arteriolitis*
 - Verminous pneumonia : inflammatory cells - consolidation & severe necrosis



Complications:

- Lung fibrosis → pulmonary hypertension (Ayerza's disease):
 - Pulmonary atherosclerosis, hypertrophy & thrombosis,
 - Pulmonary aneurism
 - Right sided heart failure
- Verminous pneumonia → fatal

Hydatid disease

Aetiology:

- **Organism:** *Echinococcus granulosus*
- **P.F. :** *Contact with infected animals (dogs, sheep, cattle)*
- **Mode of transmission :** *ingestion (contaminated food)*

Sites: Liver (65%) - Lung – muscle - brain

Gross:

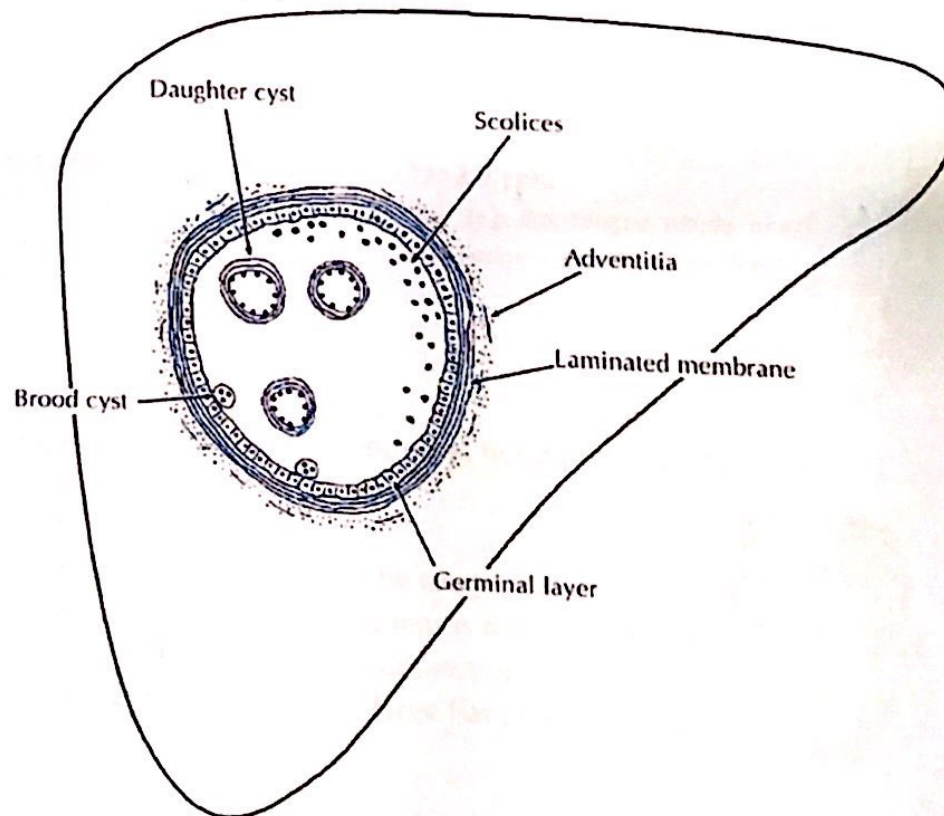
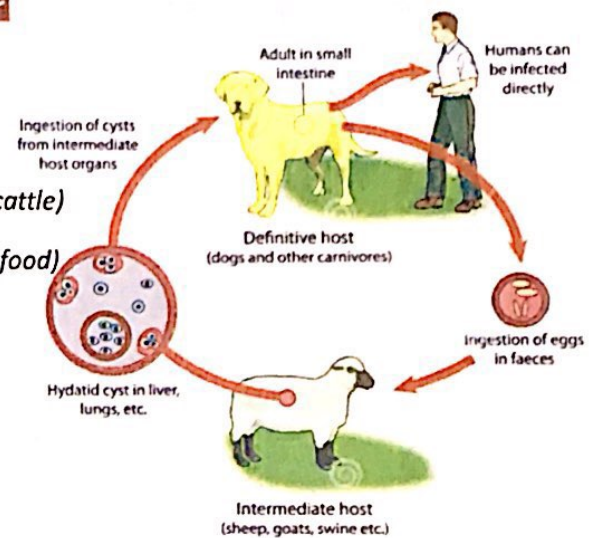
- **Shape:** rounded or oval cyst
- **Size:** 1 – 20 cm
- **C/S:** fluid – daughter cysts – white sand (calcified scolices)

Microscopic:

- Capsule (*outer laminated Acellular layer – inner nucleated layer*)
- Scolex & daughter cysts
- Surrounded by chronic inflammatory cells, excess eosinophils
- Fibrosis & Calcification

complications:

- Compression (e.g. obstructive jaundice – chest pain – bone fracture)
- Ruptured cyst → anaphylactic shock



Syphilis

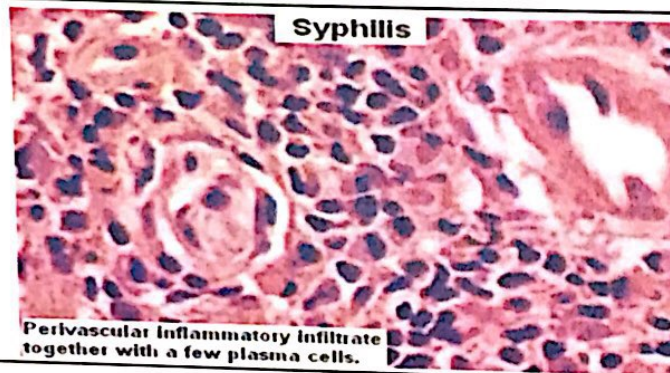
Chronic granulomatous, **venereal** disease, caused by Spirochetes (*Treponema pallidum*)

Mode of transmission

- **Contact** : e.g. sexual contact (genitals, lips, tongue) → (Acquired Syphilis)
- **Blood** : e.g. Transfusion
- **Trans-placental** → (congenital Syphilis)

Syphilitic reaction:

- **Cellular**: Chronic inflammatory cells (lymphocytes, Epithelioid, giant, fibroblasts) with excess **plasma cells**, and palisading macrophage
- **Vascular**: Plasma cell **vasculitis** → early **end arteritis** obliterans with intimal fibrosis leading to →
 - Tissue necrosis (Coagulative)
 - Granulation tissue & fibrosis
- **L.N.** :Proliferation of lymphoid tissue in LN



Acquired syphilis

(venereal: sexually transmitted)

1. Primary Syphilis (**Chancre**) after 2 weeks

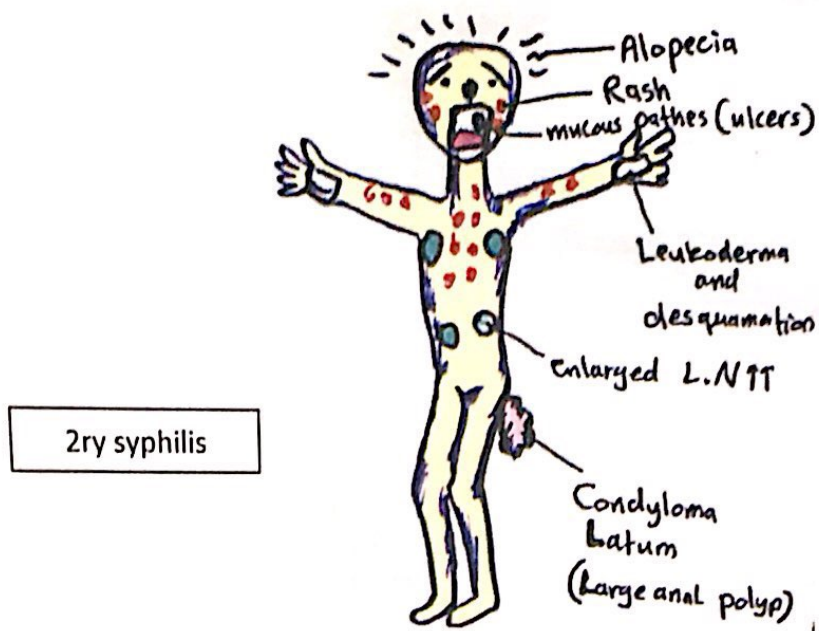
Sites: genital organ – extra genital (e.g. lips, tongue, nipple, anus)
Gross: Painless **papule** → **Ulcer** (sharp edge – pale infective floor)
Fate: Healing (no scar)



2. 2ry Syphilis (muco-cutaneous and lymphoid) after 2 months

- Alopecia
- Skin Rash
- Mucous Patches in the tongue (ulcers)
- Generalized Lymphadenitis & splenomegally
- Leukoderma & desquamation of palms
- Condyloma latum : large flat polyps (in anus)





3. Tertiary Syphilis after 2 years

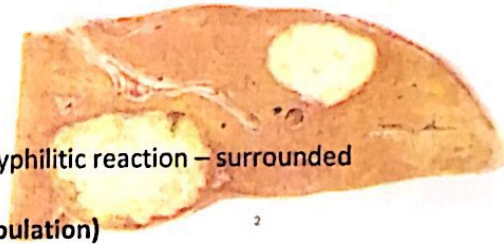
Gumma (local)

Sites: Organs (e.g. liver), , Mucosa (e.g. tongue)

Gross: irregular - rubbery - grayish white

Microscopic: Coagulative necrosis – surrounded by Syphilitic reaction – surrounded by fibrosis.

e.g. **Hepar lobatum** (gumma with scarring → liver lobulation)



Diffuse syphilitic reaction

Syphilitic Aortitis:

Site: Ascending thoracic aorta

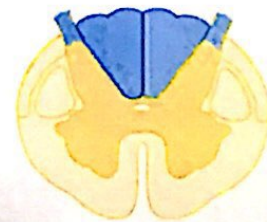
effects:

- Aneurism
- Coronary orifice stenosis
- Aortic valve prolapse



Neurosyphilis:

- Meningiovascular: Meningitis + end arteritis
- Tabes dorsalis → loss of sensation
- Generalized paralysis of insane (GPI)



Congenital syphilis

Leads to → **abortion** and **stillbirth** or **congenital anomalies** in surviving babies (**CNS lesions** – **Pneumonia Alba** - **hepato-splenomegaly** – lesions of 2ry syphilis enumerate?)



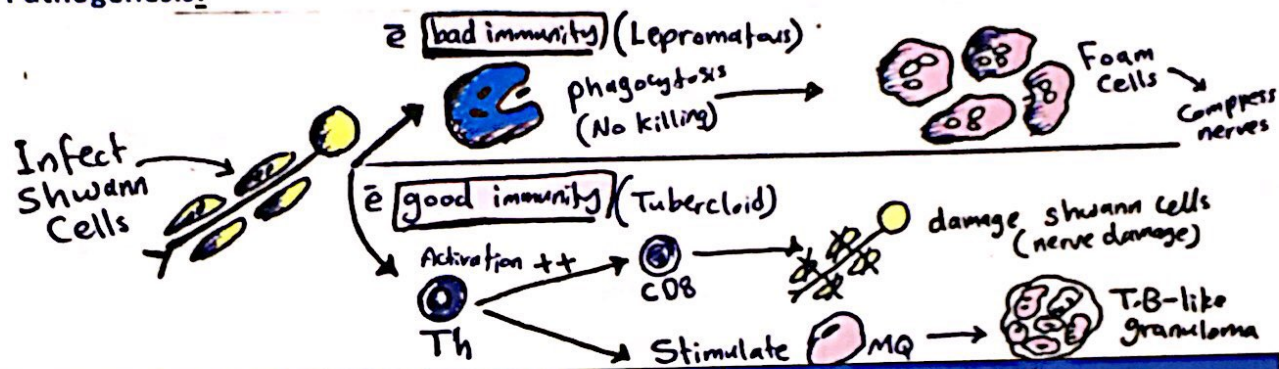
Leprosy

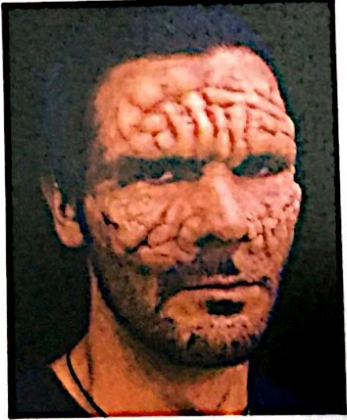
Peri-neural granulomatous disease, caused by mycobacterium lepra, which favor cold areas (skin and mucosa)

Organism: mycobacterium lepra (*acid fast*, stained by modified Z-N stain of *Fite Farco*).
Organism arranged in globules (cigarette in a pack)

Mode of transmission Inhalation : of damaged tissue containing organism → Incubation 2-20 y.

Pathogenesis:



	Lepromatous leprosy Nodular	Tubercloid leprosy Maculo-anesthetic
Immunity	Relatively lower	Relatively better
Skin	-more lesions (symmetrical) -Macules + Papules (<i>Leonine face</i>) 	-less lesions (Asymmetrical) -Anesthetic Macules (hypopigmented) 
Nerve lesion	Sensory & motor loss is less common	Sensory loss → Trophic ulcers Motor loss → e.g. ulnar palsy
Micro	-macrophage containing bacteria (foamy cells) Lepa cells -Separated from skin by clear zone (grenz zone)	- TB-like granuloma with NO caseation (describe) -the lesion is peri-neural
Lepromine test	Negative	Positive
Bacteria	more	less

Indeterminate leprosy: early stage – may heal spontaneously

Borderline leprosy: mixed type (lepromatous & tuberculoid)

Diagnosis: nasal discharge culture – Biopsy from skin – Lepramin test

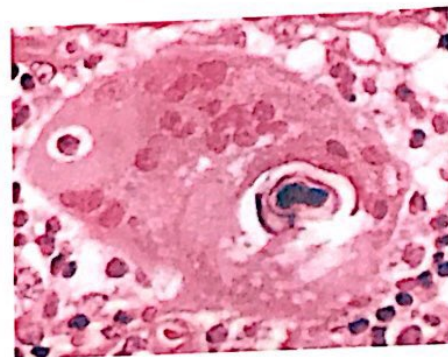
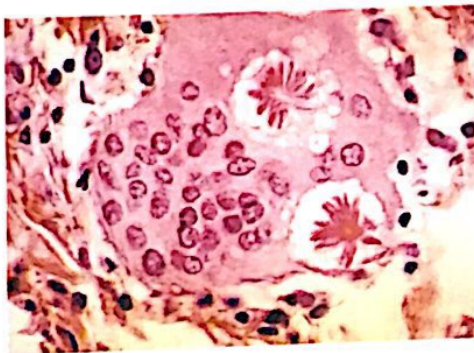
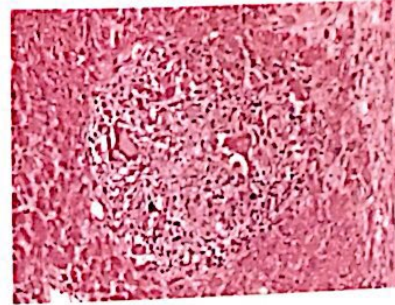
Sarcoidosis

Systemic **Non-caseating** granulomatous disease, of **unknown** aetiology

Affects males & females 20-40 y. Could be immunological or genetic

Microscopic:

- Small TB-Like granuloma (*describe?*)
- Non caseating, well defined
- Naked granuloma (No lymphocytic rim)
- Healed by fibrosis
- Inclusions inside giant cells :
 - **Astroid** bodies: eosinophilic star-shaped inclusions
 - **Schauman** bodies : Laminated concentric bodies (Ca + iron + protein)



Sites:

- **Eye (50%)** : Xerophthalmia
- **Salivary glands (parotid)** : Xerostomia. *Mickulicz disease* = Xerophthalmia + Xerostomia
- **Lung (90%)** : nodules → fibrosis → pulmonary hypertension (cor pulmonale)
- **Hilar & tracheal L.N.**: bilateral, large, firm & discrete → compress bronchi → dyspnea
- **Skin (25%)** : Violaceous plaques in face – **Erythema** nodosum (red tender in the leg)
- **Hepato - splenomegaly**
- **Bone & bone marrow (40%)** : mainly short bones → radiolucent lesions

Fate: 70%: recovery, 20%: Lung Fibrosis, 10%: Cor pulmonale 10%: ocular complications

Diagnosis: Clinical – Exclusion of TB – LN or lung biopsy - elevated ACE & vit D (secreted by macrophage), hypercalcemia

Actinomyces

Suppurative Chronic granulomatous disease, caused by actinomyces

- **Organism:** Actinomyces Israelii (anaerobic flora of oro-pharynx, vagina and intestine)
- **P.F.:** Mucosal injury

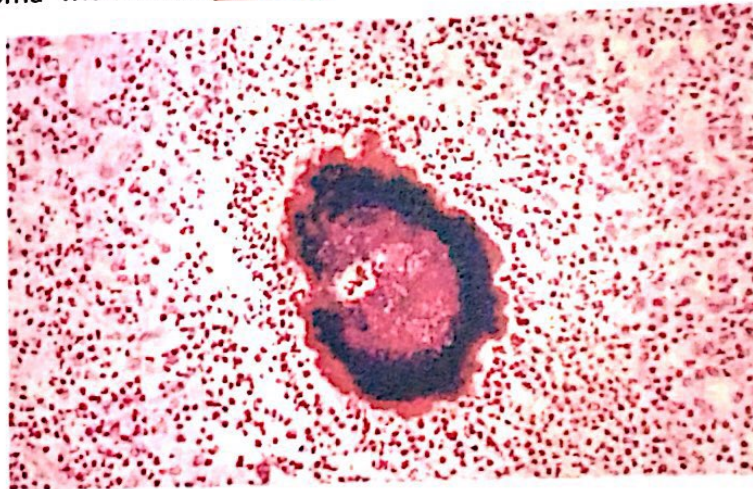
Gross:

- Multiple abscesses with multiple sinuses
- Pus is thick, yellow 'sulphur granules'
- L.N enlargement is **not common** (due to thick pus containing large colonies)



Microscopic:

- Bacterial filaments (basophilic), surrounded by acidophilic clubs (Ig)
- Surrounded by mixed granuloma with excess pus cells
- Granulation tissue & fibrosis



Types:

- **Cervico-Facial 60%**
 - After injury of oral mucosa (e.g. traumatic ulcer, dental lesions)
 - Gross (as described) , Micro (as described)
- **Intestinal (Abdominal)**
 - After injury of intestinal mucosa (e.g. ulceration), or swallowing oral pus
 - Appendix – cecum - ileum
 - Spread → portal blood → honey comb Liver → spread to diaphragm → Lung
 - direct → peritonitis → open into abdominal . wall → skin sinuses
- **Thoracic**
 - From blood spread - oral aspiration – or spread directly from liver
 - Affect the base of the lung
 - Pleural spread → empyema → open into chest wall → sinuses
- **Pelvic** in females associated with IUCD



Mycetoma

- **Organism:** **Bacterial** Mycetoma (actinomyces nocardia) or **Fungal** EuMycetoma (Madurella)
- **P.F.:** Bare **Skin injury** (hand-foot – shoulder) + contaminated with **soil**

Gross:

- Swelling with multiple sinuses
- 'sulphur granules' Pus is thick, **yellow** (**bacterial**) or **black** (**fungal**)
- Bone and muscle necrosis

Microscopic: similar to actinomycosis



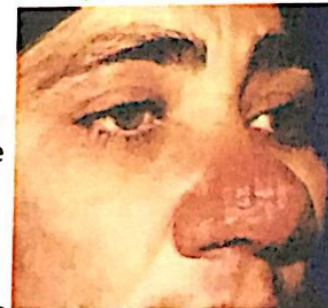
Rhinoscleroma

Chronic granulomatous disease, caused by **Klebsiella** Rhinoscleromatous
More in females 20 -40 y

Mode of transmission: Inhalation → rhinoscleroma, laryngeoscleroma, pharyngeoscleroma,

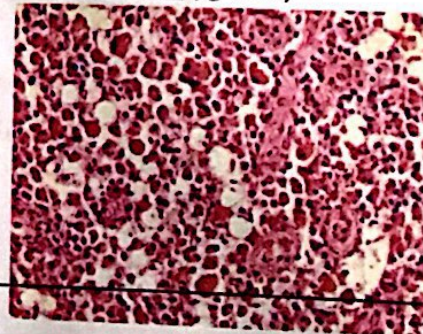
Gross:

- waxy granules → rounded **nodule**
- **Destructive** lesion: compression & destruction of surrounding tissue
- **Deformity:** healing by fibrosis & scar formation



Microscopic:

- Covering epithelium: Ulceration – **epitheliomatous Hyperplasia** – Squamous metaplasia
- Core :
 - Chronic inflammatory cells (lymphocytes, plasma, macrophage) with:
 - **Mickulicz cells** : Numerous macrophage with foamy cytoplasm, containing bacteria
 - **Russel bodies**: hyalinized eosinophilic plasma cells (Ig- rich)
 - Granulation tissue
 - Fibrosis (later)



Clinical: slowly progressive

- Rhinitis
- Anosmia
- Hoarseness of voice & Asphyxia

Filariasis

Chronic granulomatous disease, caused by *Wucheraria Bancrofti* parasite

Mode of transmission: Culex mosquito → parasite infects Lymphatics & L.N.s

Microscopic:

- Dead worm – surrounded by inflammatory cells & eosinophils
- Lymphangitis
- Lymphangectasia (dilated lymph vessels)

Clinical:

Acute Fever – eosinophilia – Lymphadenitis – Orchitis

Chronic:

- Lymphedema: in Lower limb – arms – genitals
- Elephantiasis: Thick firm skin due to 2ry infection & fibrosis
- Hydrocele
- Lymphadenitis: Inguinal & femoral
- Subcutaneous nodules: Inflammatory reaction around dead worm



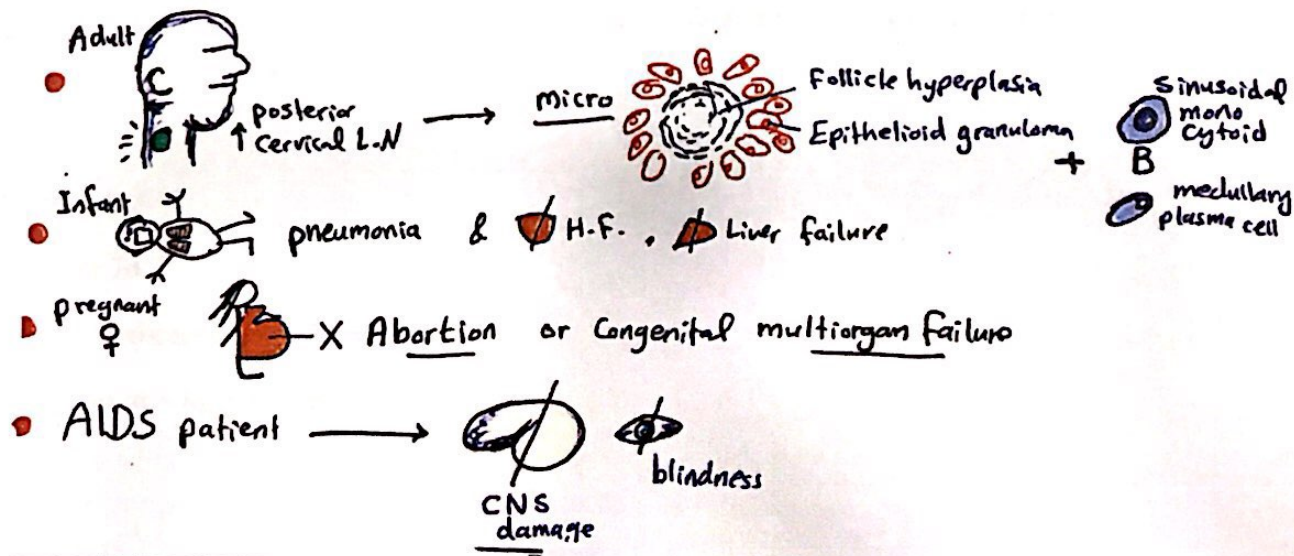
Toxoplasmosis

Chronic granulomatous disease, caused by *Toxoplasma gondii* parasite



Mode of transmission: ingestion of contaminated food or meat (cats are carrier)

Pathological effects:



Give reason:

- Extensive tissue caseation in 2ry TB
- Less L.N. enlargement in 2ry TB
- Minimal caseation in miliary TB
- Caseation in TB granuloma
- Portal hypertension in hepatic bilharziasis
- Urinary bilharziasis may predispose to cancer bladder
- Renal failure in case of old urinary bilharziasis

Complete:

1-Skin reaction to Cercaria is mediated byhypersensetivity, while granulomatous reaction is mediated byhypersensitivity.

2-Tuberclin test is positive in and

3-Multiple small uniform of TB foci are seen in T.B.

4-The commonest cause of death in complicated hepatic bilharziasis is.....

5-.....is a dipping mass of transitional epithelium

6-Cystitis glandularis may predispose to while Squamous dysplasia is predisposing to

7-Fibro-sidrotic nodules in splenic bilharziasis are named.....

8-1ry pulmonary complex is composed of,, &

9-Causes of bilharzial ulcers include.....,, &.....

10-Gohn's focus is found in.....of the lung, while Assman's focus is found inof the lung.

Caompare:

1ry – 2ry TB

Chronic fibrocaseous – Miliary TB

Gohn's focus – Assman's focus

True/ False:

- 1- Regional lymph node is commonly enlarged in actinomycosis ()
- 2- Lymph node enlargement is extensive in 2ry TB ()
- 3- Sandy patches are areas of atrophic granular mucosa ()

Complete

- 1- The most common site of Syphilitic periostitis is
- 2- The pathognomonic cell of Rhinoscleroma.....
- 3- The edges of T.B ulcer are.....
- 4- Types of Bilharzial polyps And.....
- 5- Miliary TB is fatal due to.....
- 6- Elephantiasis is caused by.....
- 7- Causes of pulmonary actinomycosis include.....,.....,
- 8- Sarcoid granuloma is showing calcified inclusion which is named.....
- 9- TB-Like , non-caseating granuloma is found in and
- 10- Perineural granuloma is a characteristic feature of.....
- 11- Plasma cell vasculitis is seen in.....
- 12- Chancre is the primary lesion of
- 13- Gumma is formed of,,
- 14- Pneumonia alba is found in syphilis
- 15- Condyloma latum is found insyphilis
- 16- Granuloma which is not caused by infection
- 17- Fungal granuloma is seen in.....
- 18- Parasitic granuloma which is transmitted by cat feces is.....
- 19- Eosinophilic clubs in actinomycosis are formed of.....
- 20- Russel bodies are hyalinized.....cells
- 21- Direction of Ulcers in secondary intestinal TB is
- 22- Precancerous parasitic granuloma
- 23- Vitamin D is secreted by..... In sarcoidosis
- 24- The commonest site of Actinomycosis is
- 25- Pelvic actinomycosis is predisposed by.....
- 26- Leprosin test is in tubercloid leprosy
- 27- Leonine face is associated with
- 28- Leprosy is transmitted by.....
- 29- Mycobacterium lepra is primarily infecting.....cells
- 30- Asteroid bodies are seen in.....

Discuss: Pathogenesis of Cavitation in 2ry T.B

.....

.....

.....

.....

Explain (Give reason for):

Tabes mesenterica:.....

.....

Trophic lesions in Leprosy:.....

.....

Swollen limb in filariasis

.....

.....

MCQ:

1-Sarcoidosis is

a-Granulomatous inflammation

b-Caseating granuloma

c- Diagnosed by sputum culture

d- showing hypocalcemia

2-Granuloma is commonly seen in the following lesions (Except) :

a-Gohn's focus

b-Splenic bilharziasis

c-Tubercloid leprosy

d-Lepromatous leprosy

3-The commonest site of 1ry pulmonary focus is:

a-Apex of the right lung

b-Apex of the left lung

c- Base of the left lung

d- non of the above

4-The following are complications of Bilharzial portal hypertension (except):

a-Liver cirrhosis

b-Hematemesis

c- Ascitis

d- Pulmonary bilharziasis

5-Mickulikz cell is:

a-plasma cell

b-Epithelioid cell

c- Macrophage

d- non of the above

Compare:

1ry -2ryintestini TB

Lepromatous leprosy – Tubercloid leprosy

Sarcoid granuloma – TB granuloma

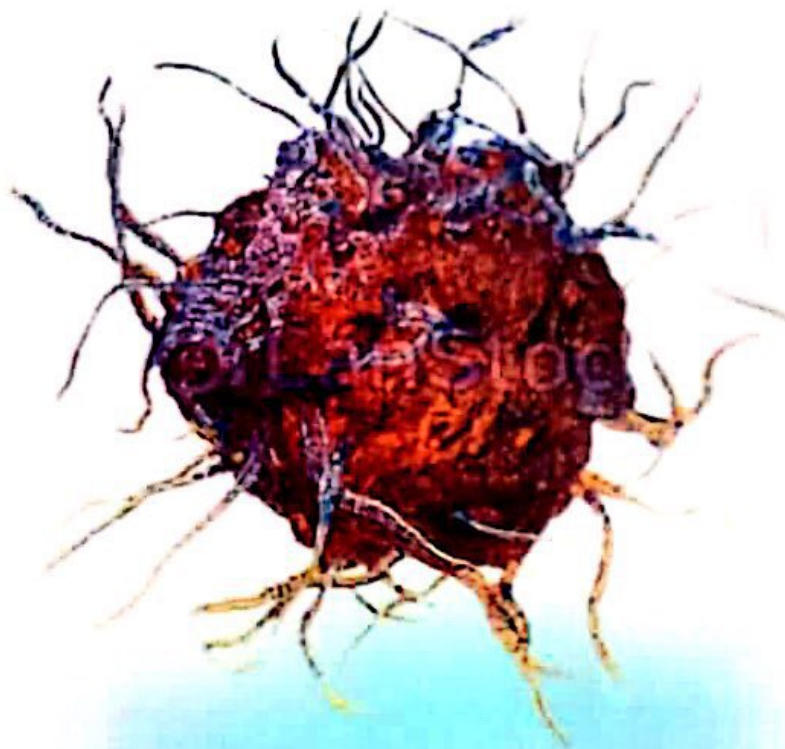
Actinomycosis – Mycetoma (organism – sites – gross)



Easy PATHOLOGY

Dr. Abdelrahman Khalifa

Immunity



2018 -2019

Auto immune diseases

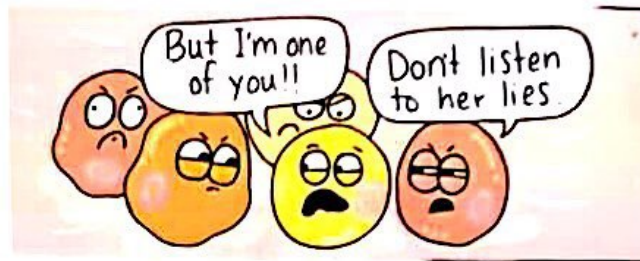
Immunological reaction against self Ag (loss of tolerance)

Pathogenesis:

Inheritance , Infections, or acquired factors leading to → abnormality in tolerance :

- **Central tolerance:** Apoptosis of T cells and B cells in B.M. & Thymus
- **Peripheral suppression (anergy) :** suppression by regulatory T-cells or apoptosis

The previous mechanisms are broken in Autoimmune diseases



Types:

Single organ or cell type	Systemic
Hashimoto's thyroiditis	Systemic lupus erythematosus
Autoimmune hemolytic anemia	Rheumatoid arthritis
Autoimmune atrophic gastritis	Sjogren syndrome
Good pasture syndrome	Systemic sclerosis
Type I diabetes mellitus	Polyarteritis nodosa
Graves disease	
Ulcerative colitis	
Primary biliary cirrhosis	

Systemic Lupus Erythematosus (SLE)

Autoimmune diseases affecting multiple organs, more common in females

Female > male (9:1), affecting middle age

Aetiology

- Genetic factor
- **U.V.** → apoptosis of epidermal cells → formation of nuclear Ag
- Drugs (hydralazine)
- Female sex hormone



Pathogenesis

Formation of **Auto Ab** (Anti nuclear ANA, AntiDNA, Anti smith) → **type III hypersensitivity**
→ vasculitis, fibrinoid necrosis & tissue necrosis

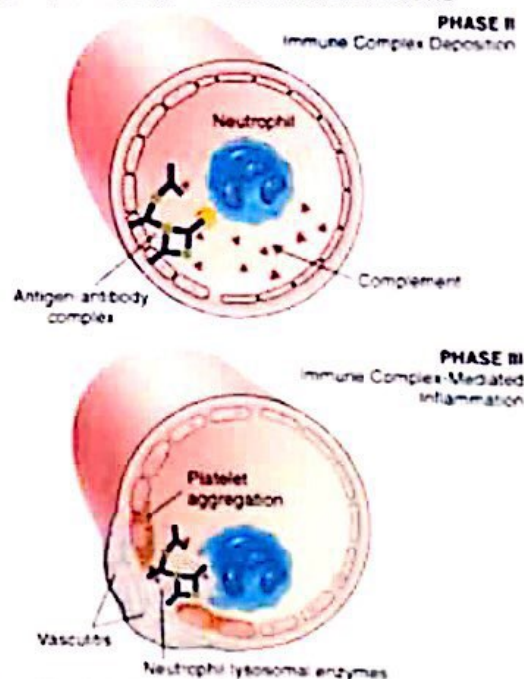
Pathological features:

- CNS → Neuropsychiatric disorders
- Skin → Malar (**butterfly rash**), exaggerated with U.V.
- Heart → **Endocarditis** & vegetations (*Libman sack endocarditis*), pericarditis
- Serous sacs → S.F. inflammation
- Vessels → necrotizing vasculitis
- Kidney → Lupus nephropathy & G.N. → **Renal failure** is the common cause of death
- Splenomegaly (hyperplasia of follicles + arteriolar fibrosis '**onion skin**')
- Joints → **Arthritis** (Synovitis)

Diagnosis:

- Clinical
- Lab: Auto antibodies (elevated ANA, low levels of complement)
- Renal biopsy & urine sample (hematuria & proteinuria)
- **Renal function** for follow up

Causes of death: **Renal failure** – Infections – diffuse CNS lesions



Type III hypersensitivity

Lupus nephropathy (text)

deposition of DNA-anti-DNA complexes within the glomeruli → glomerulonephritis
→ proliferation of the **endothelial**, **mesangial**, and/or **epithelial** cells and

in severe cases → **necrosis** of the glomeruli.

class I, minimal **mesangial** lupus nephritis

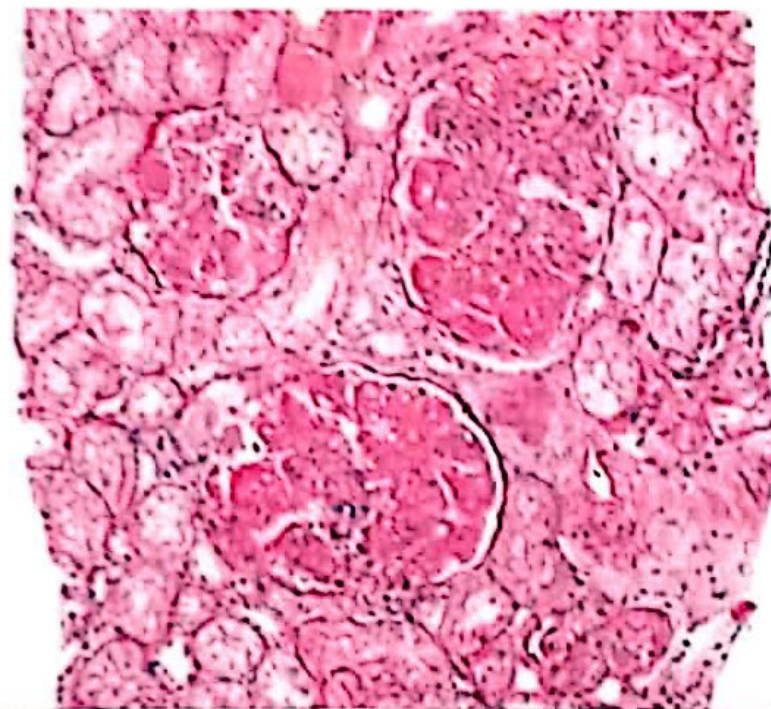
class II, **mesangial** proliferative lupus nephritis

class III, **focal** lupus nephritis

class IV, **diffuse** lupus nephritis (the most common, the most serious)
characterized by Crescent formation → **Wire-loop** appearance
Clinically : Hematuria, proteinuria and hypertension

class V, membranous lupus nephritis

class VI, sclerosing lupus nephritis.



Amyloidosis

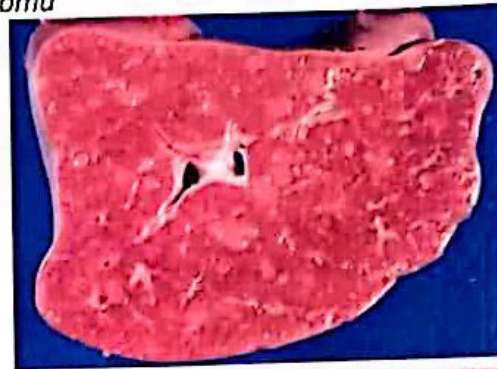
Extracellular accumulation of abnormal homogenous eosinophilic abnormal amyloid protein.

Composition: Glycoprotein (5%) + Fibril protein (95%) nonbranching, misfolded, insoluble

- **AL** (Amyloid light chain): secreted by Plasma cells (Light chain Ig)
- **AA** (Amyloid associated): Present in serum, secreted by liver
- **Transthyretin** found in Senile Amyloidosis, & familial neuropathy
- **Beta2 mgb** in prolonged hemodialysis
- **Beta Amyloid** in Alzheimer, & medullary carcinoma

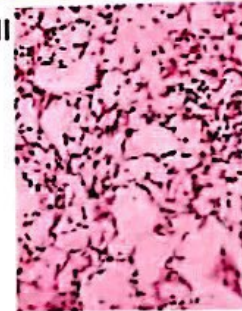
Gross:

- **Stain:** Blue (with iodine + 1% H₂SO₄)
- **Size:** increased
- **Shape:** sharp borders
- **Color:** waxy, pale brown deposit
- **Consistency:** firm



Microscopic:

- **Deposit:** Homogenous, glossy, eosinophilic, in CT, and Blood vessel wall
- **Staining of amyloid:**
 - H&E → pink
 - Congo red → orange red → green with polarized light



Renal amyloidosis:

The most commonly affected organ. Deposits are seen in:

- Arterioles → ischemia → R.F. & hypertension
- Glomeruli → proteinuria → Nephrotic syndrome

Liver amyloidosis: Deposits are seen in sinusoids & space of diss → hepatomegaly

Intestinal amyloidosis: In the basement membrane → malabsorption

Cardiac amyloidosis:

- Deposits are seen Interstitial between muscle fibers
- Restrictive cardiomyopathy in late stages

Splenic amyloidosis:

	Sago Spleen	Diffuse amyloidosis
Microscopic	Deposits in central arterioles & follicles (white pulp)	Deposits affect sinusoids (red pulp)
Gross	-Moderate enlargement -waxy nodules	-Marked enlargement -Waxy cut section

Types of Amyloidosis:

- **Localized** (deposit in single organ)
 - Thyroid medullary carcinoma (A. calcitonin)
 - Senile Cardiac amyloidosis
- **Systemic**: (circulate in blood & deposit in multiple organs)

- **Primary: (AL)**



- **Multiple Myeloma** (plasma cell tumor)
- **Pathogenesis**: malignant plasma cell → AL protein → circulate in blood → deposit in organs
- **Organs affected**: Kidney, heart, GIT, Nerves ...etc.
- **Bence – jones** protein in urine

- **Secondary: (SAA)**



- **Aetiology**: (chronic destructive diseases)
 - Chronic suppurative (e.g. Lung abscess)
 - Chronic granuloma (e.g. T.B)
 - Autoimmune diseases (e.g. Rheumatoid)
 - Cancers (Hodgkin Lymphoma)
- **Pathogenesis**: Chronic destructive disease → macrophage accumulation and stimulation → secrete Cytokines (CK) → circulate in blood → affect Liver → Liver secrete (AA) → circulate in blood (SAA) → deposit in multiple organs
- **Organs affected**: Kidney, heart, GIT, Spleen, Liver
- **Cause of death**: Renal failure

- **Hemodialysis-associated**

- (B2 mgb) → carpal tunnel syndrome

- **Hereditary**

- Familial Mediterranean Fever: AA
- Familial polyneuropathy: ATtr

Prognosis of amyloidosis :

Poor in systemic Amyloidosis (R.F., H.F.)

Poor in 1ry ayloidosis (requires chemotherapy)

Diagnosis of amyloidosis:

- Clinical
- Biopsy + Congo red staining
- Rectal and gingival biopsy specimens contain amyloid in up to 75% of cases with generalized amyloidosis.

Type of disease	Disease	Type of protein
Systemic: 1ry (Immunocyte disease)	Multiple myeloma	AL
Systemic: 2ry (reactive)	Chronic inflammation	AA
Systemic: Hemodialysis	Renal failure	Amyloid B2 mg
Systemic: Hereditary	Familial medetr, fever	AA
Systemic: Hereditary	Familial neuropathy	ATtr (amyloid transthyretin)
Systemic: Hereditary	Systemic senile	ATtr (amyloid transthyretin)
Localized: Cerebral	Alzheimer	AB
Localized: Endocrinal	Medullary carcinoma thyroid	A. Calcitonin

a)Hepatic b)Pancreatic
c)Renal d)Splenic

a)Osmic acid
c)Masson trichrome

b)Sudan III
d)Congo Red

a) Intracellular perineuclear b) Intracytoplasmic
c) Glandular Intraluminal d) Extracellular

a) T.B.
c) Rheumatoid artheritis

b) Chronic lung abscess
d) All of the above

a) Hyalinosis b) Multiple myeloma
c) AL amyloidosis d) Localized Amyloidosis

a) Rheumatic fever b) Rheumatoid arthritis
c) SLE d) All of the above

a) Hashimoto's thyroiditis b) Ulcerative colitis
c) Arthus reaction d) Good pasture's disease

a) ANA b) Renal function
c) IgE measurement d) Non

Cases1:

A young girl is complaining of chest pain during inspiration, Pink discoloration of cheeks & nasal skin. Urine analysis revealed proteinurea. Serum ANA level is elevated.

- 1-Diagnosis
- 2-Explain chest pain
- 3-Pathogenesis
- 4- What is the aim of follow up ?

Cases2:

Old female with history of rheumatoid artheritis. She came with periorbital edema and lower limb edema.

- 1-Diagnosis
- 2-What is the aim of biopsy & stain required?
- 3-Pathogenesis of edema
- 4- List other expected systemic complications ?

Cases3:

Old male is complaining of pulmonary TB for more than 2 years. Now he has generalized edema and proteinurea. Both kidneys are enlarged.

- 1-Diagnosis
- 2-Gross & microscopic picture of the kidney?
- 3-Fate ?

Q1: B-lymphocytes are the main effector cells in the following diseases EXCEPT:

- a) Urticaria
- b) Systemic lupus erythematosus
- c) Bronchial asthma
- d) Tuberculosis
- e) Autoimmune haemolytic anaemia

Q2: Kidney function tests may be affected in all these diseases EXCEPT:

- a) Rheumatoid arthritis
- b) Tuberculosis
- c) Systemic lupus erythematosus
- d) Viral pneumonia
- e) Hodgkin's lymphoma

Q3: A 20 years old girl presents by chest pain related to breathing and right knee arthralgia. Her family doctor noticed pinkish cheeks with no artificial make up . She was diagnosed and submitted to regular follow up. The patient can afford single test on regular follow up , which one do you chose ?

- a) Liver function tests
- b) Serum ANA
- c) Respiratory function tests
- d) Renal function tests
- e) ECG

Q4: SLE is mediated by:

- a) Type I hypersensitivity
- b) B- Type II hypersensitivity
- c) C- Type III hypersensitivity or

d) D- Cell mediated immunity

Q5: Sago spleen denotes:

- a) Congestion within red pulp
- b) Multiple splenic infarcts
- c) Amyloid deposition in white pulp
- d) Amyloid deposition in red pulp
- e) Reactive hyperplasia of white pulp

Q6: Autopsy of an elderly individual who died in a nursing home with no known genetic diseases reveals small amounts of amyloid deposition in the heart. Amyloid deposition is not seen in other organs. There is no history of long-standing inflammatory disease. This type of amyloid would be most likely composed of which of the following proteins?

- a) Amyloid-associated protein.
- b) Amyloid light chain protein
- c) Beta-2-amyloid protein
- d) Beta-2-microglobulin
- e) Transthyretin

Q7: A 54 years male patient with old history of pulmonary TB presents by generalized oedema. Urine analysis reveals proteinuria. Renal biopsy reveals deposition of pale eosinophilic material within the glomeruli and wall of blood vessels. The best stain chosen would be:

- a) Ziel-Neelsen stain
- b) Masson trichrome
- c) Congo red
- d) PAS
- e) Haematoxylin & Eosin

Q8: The commonest cause of death from generalized Secondary amyloidosis is:

- a) Left sided heart failure
- b) Renal failure
- c) Septic shock
- d) Cerebral stroke
- e) Liver cell failure

Q9: Bence-Jones proteins are detected in urine of patients Suffering of:

- a) Chronic renal failure
- b) Urinary bladder Bilharziasis
- c) Alzheimer's disease
- d) Multiple myeloma
- e) Renal cell carcinoma

Q10: Biopsy from an 85 years old lady with progressive symptoms of dementia reveal deposition of homogenous pale pink material in wall of cerebral vessels. This material was polarizing when stained with congo red . Of which of these substances this material is composed ?

- a) Collagen
- b) Transthyretin
- c) Calcium phosphate
- d) A β amyloid
- e) Calcitonin

Q11: In SLE, the pathological change that may affect joints is In the form of:

- a) Acute suppurative inflammation
- b) Crystalloid deposition
- c) Acute serous inflammation
- d) Chronic non specific inflammation
- e) Degenerative changes